# TRANSACTIONS

OF

# The Association of Life Insurance Medical Directors of America

SIXTY-THIRD ANNUAL MEETING

James R. Gudger, M. D.
*Editor*

VOL. XXXVIII

PRESS OF
Recording & Statistical Corporation
New York City
1955

Printed in U. S. A.

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# Transactions of The Association of Life Insurance Medical Directors of America

## SIXTY-THIRD ANNUAL MEETING

The Sixty-third Annual Meeting of The Association of Life Insurance Medical Directors of America, held at the Royal York Hotel, Toronto, Ontario, Canada, convened at ten-fifty o'clock, Dr. Richard C. Montgomery, President of the Association, presiding.

PRESIDENT MONTGOMERY — Before proceeding with the first Scientific Meeting, we shall have a word from our old friend James P. Donelan, Chairman of the Medical Section of the American Life Convention, who will bring us greetings.

DR. JAMES P. DONELAN — Mr. President, fellow members and guests: It is a real pleasure to be here with you in Toronto and to bring you greetings from the Medical Section of the American Life Convention. I am also grateful for the opportunity of inviting all of you to our Annual Meeting next June.

Dr. John Boland, our Program Chairman, is hard at work and from the commitments to date I can promise you a three-day session that should run second to none from a practical and informative standpoint. The meeting will be held at the Homestead in Hot Springs, Virginia on June 27, 28 and 29. Hot Springs, as you know, is a delightful spot and our schedule provides ample time for recreational activities — golf, tennis — as well as the opportunity to relax and enjoy good fellowship with old friends and new acquaintances.

We hope all of you will make an earnest effort to be with us in Hot Springs next June.

PRESIDENT MONTGOMERY — Thank you, Dr. Donelan.

Now, an old friend of ours, Dr. Francis Dieuaide, will talk to us about the Life Insurance Medical Research Fund. We are always glad to hear from Dr. Dieuaide.

DR. FRANCIS DIEUAIDE — Mr. President and members of the Association: A new Annual Report of the Life Insurance Medical Research Fund will be distributed within the next two weeks. In addition to the full report, a brief condensed report is widely circulated which serves the useful purpose of informing laymen about the work of the Fund. We believe you will find these publications interesting. We ask your help in getting them into the hands of others who may be interested.

Contributions to the Fund for 1954 amount to just over $900,000. There are this year 142 member companies.

During 1953–54 the Fund supported 88 research programs and 37 research fellowships, all devoted directly or indirectly to cardiovascular disease. The awards were widely distributed throughout the United States and Canada.

A great deal of new information has been provided which relates to the pathogenesis of arteriosclerosis, and hence of coronary artery disease. A number of methods have been found by which cholesterol production in the body and cholesterol deposition in the arteries can be controlled experimentally. Five years ago, these processes were commonly regarded as immutable. Today, we can look forward to the development of a practically useful method of control.

I firmly believe we can also expect in a reasonable time, a solution to the outstanding problem of the significance of the fat intake in the causation of arteriosclerosis.

A number of new drugs have been tested in the treatment of hypertension and found to be potent depressors of blood pressure. Responses have been obtained in some cases of malignant hypertension previously beyond relief. These new agents have considerably improved the physician's ability to help hypertensive patients, even though they have serious limitations. Better drugs will be forthcoming.

On the etiological side, we can report the isolation from human urine of a new and powerful blood pressure-raising substance.

Further knowledge of this substance may revolutionize our ideas about the mechanism of essential hypertension.

In connection with the clinical management of patients, the Fund is aiding in the basic development of a better method for ballistocardiography. This procedure, hitherto difficult of application and uncertain in interpretation, demands exploitation, because it aims at a vital function otherwise not accessible, namely the force of the heart beat.

Another difficult, but important development is that of the so-called mechanical heart. With a more nearly perfect apparatus, cardiovascular surgery will be greatly improved and operations can be undertaken which are now impossible.

The present productivity and vigor of heart research are most encouraging. Ten years ago, work toward the control of cardiovascular disease was generally neglected and viewed as hopeless. Today the outlook is truly promising. Through the Fund, life insurance deserves credit for no small part of this favorable development.

PRESIDENT MONTGOMERY — Thank you, Dr. Dieuaide. We are always glad to hear from you.

Ladies and gentlemen, it is a pleasure for me to welcome all of you to Toronto to attend the Sixty-third Annual Meeting of the Association.

On looking back over the records, our good friend Dr. Dewis brought out a program which had been used when this group had its last meeting in Canada. That was in 1933. The date was the 12th and 13th of October, and the place, the Royal York Hotel. The President, on that occasion, was Dr. Crawford Scadding, of the Canada Life Assurance Company. The last Canadian who presided over these meetings is Dr. Samuel Streight, also of the Canada Life. We are very glad that we could have these two members with us today, along with other retired Presidents.

Since 1933 there have been great changes in underwriting. We have come a long way. We now offer insurance to more people than ever before and probably on a better basis. This is partly due to advances in medicine along all lines, partly due to better

mortality in the population, but partly also to the fact that we can now examine our clients more thoroughly than ever before. It goes without saying that if we are to continue to advance, we must take care to select as well as possible. There is only one point concerning this matter which I would like to emphasize. If we are able to learn as much, or even a little more, than the client knows about himself, we will be able to underwrite substandard risks successfully. However, if we know a little less about our clients than they know about themselves, we will be running into trouble. Careful selection would seem to be the answer to underwriting any risk but especially those risks who are below normal.

I am sure you will agree that our Committee has provided us with an excellent Scientific Program to which we will proceed without any further remarks from me.

Our first speaker this morning on our Scientific Program is Dr. Ray F. Farquharson. Dr. Farquharson's ancestors lived and loved, fought and ruled in Aberdeenshire over the past centuries. He is a son of the Presbyterian Manse. One of his ancestors fought with Wolfe on the Plains of Abraham, and another, on his mother's side, a Captain McDonald, was in a Highland Regiment and thrown out of Boston during the American Revolutionary War. It is fitting, therefore, that nearly a century and a half later Dr. Ray Farquharson went back to Boston for some of his post-graduate work. He was a private in the Canadian Army in 1914–18, and consultant to the Royal Canadian Air Force in medicine in the recent World War II. He took training in Canada, England and the United States. Dr. Farquharson is at present Professor of Medicine in the University of Toronto.

I assure you I have a great deal of pleasure in calling on Dr. Ray Farquharson to give us our first paper.

# THE PRESENT MEDICAL SITUATION

RAY F. FARQUHARSON, M.B.E., M.B., M.R.C.P. (Lond.), F.R.C.P.(C)

*Professor of Medicine*
*University of Toronto*

In considering the present medical situation it is interesting, and actually necessary, to look at it from a point of view different from our own. When I was trying to do so during the past summer I had great pleasure in reading Sir Charles Sherrington's Life of Jean Fernel[1] who lived and thought and practised medicine almost five hundred years ago. He published the first texts of physiology and pathology as part of his System of Medicine. An early humanist, he began the practice of medicine with a firm belief in astrology and he studied mathematics in order to understand better the movements of the stars. In years of practice, however, his own observations gradually convinced him that the state of the heavens bore no constant relationship to the ills of his patients and that diseases were due to natural causes.

The complicated mixtures of drugs which he used have long since been forgotten and were he able to view present day methods of treatment he might find nothing with which he was familiar except, perhaps, the use of opium and mercury. One quality, however, in which, like all great physicians, he excelled was his genuine interest in and sympathy for his patients. A contemporary physician remarked with wonder on his kindly and sympathetic inquiry into their slightest symptoms and noted that he was also interested in everything they did and in their opinions. He won the confidence of all and acquired a great reputation throughout Europe. King Henry II of France declared that as long as Fernel was beside him he knew that no illness would be mortal.

Could Fernel view our medical situation from the point of view of his own experience he would be amazed at the advance in useful technic. He would find it hard to credit the virtual disappearance of many diseases, the rapid cures of others, the almost unbelievable advances in surgery and the changes in basic medical knowledge.

Perhaps his philosophy would make it easy for him to understand that when illnesses are prevented or cured by simple technics there is little gratitude on the part of the patient, for he would know that the prestige of the physician and the affection felt for him by his patients depend not so much on results as on his personal interest and the support given them in time of suffering. He would realize that the prestige of medical science was assured and never could be undermined. Actually it has never been doubted. He would, however, be aware of the danger that some individual physicians might pay too much attention to important technical methods of diagnosis and treatment, failing to appreciate that the scientific medicine always requires a broader outlook and that kindly interest and support are wonderfully effective in treatment of most patients.

Today I should like to discuss the present medical situation not from the point of view of Fernel or any other previous great physician, for that would be impossible, yet keeping their experiences in mind to do so as objectively as I can. At best it must be a superficial and inadequate survey; many important aspects must be left unmentioned, and perhaps it is too big a subject even to be attempted. I shall, however, proceed dealing with groups of disorders rather than with special fields of knowledge or technic, and shall begin with infections.

*Infections*

The role of sanitation in the prevention of infections can hardly be overestimated. Beginning prior to the modern knowledge of bacteriology and continuing since that time, improvements in sanitation associated with greater prosperity have led to the virtual disappearance in Europe and western countries of many diseases that still flourish in the East and are called tropical diseases[2]. To eradicate them in the world will require a great advance in prosperity and social organization among poverty-stricken people. In our countries the great results of sanitation have been achieved; the problems are not all settled, but the great part of the work in prevention of illness has been accomplished.

Prevention of disease by vaccination is still an active problem. The success of smallpox vaccine naturally led to the hope that

those infections, one attack of which confers lasting immunity, might similarly be prevented. Good results have been obtained when attenuated living vaccines have been used, as in the case of yellow fever and a number of veterinary diseases. The use of toxoids in the prevention of diphtheria and tetanus has been equally successful. The administration of BCG has resulted in a favorable influence on the resistance of persons exposed to tuberculous infection; unfortunately it is a partial and an imperfect measure. But the injection of killed cultures, as in the case of typhoid and pertussis and many other vaccines, has been associated at best with temporary and partial immunity, sometimes perhaps with amelioration of the severity of the disease, and often has been of no value whatsoever. One may hope that a high concentration of killed virus, as in the poliomyelitis vaccine currently being tried, may induce a higher and more lasting grade of immunity than has attended the administration of other killed vaccines, but that remains to be seen. There is great hope for the future of preventing those severe infections that confer subsequent immunity by the development of safe attenuated living vaccines. Until that time comes, and for all the serious infections that tend to recur again and again, successful treatment with prevention of complications will depend largely on the use of chemotherapeutic agents.

The history of the development of antibiotics and other useful chemotherapeutic agents is an interesting matter which we have not time to discuss. Of all these remedies penicillin still holds first place. It is bacteriostatic at all times and it is bacteriocidal also during cell division. Like all antibiotics, it is effective only when it can be brought in contact with the sensitive infecting organism in the tissues. Accordingly it does not replace needed surgical measures such as the drainage of abscesses or the saucerization of infected bone and removal of sequestrae or other medical measures including great increase in the ordinary dosage usually used in an attempt to bring an adequate concentration to the infecting organism in bloodless tissues such as thrombi on heart valves and some lesions in the meninges and pleural cavities. It is a wonderfully useful antibiotic because it is usually effective in relatively small concentrations against the common pathogenic organisms — pneumococci, streptococci, gonococci, meningococci and the spiro-

chaete of syphilis. Fortunately none of these organisms have tended to become resistant to its effects and, since the common infections which they cause occur usually in tissues well supplied with blood vessels which carry the antibiotic to the site of the lesion, the results of therapy are prompt and dramatic. The general use of penicillin has reduced the incidence of syphilis tremendously and has led to rapid recovery without complications in cases of gonococcal urethritis. Whether it has reduced the incidence of pneumococcal and streptococcal infections or not is hard to tell, but it has led to such rapid cure in acute cases that these diseases have ceased to be dreaded. Unfortunately pathogenic staphylococci have a tendency to develop resistance not only to penicillin but to all other antibiotics so far introduced, and staphylococcic infections are still matters of great concern. It is usually possible, by isolating the organism and testing the whole range of modern antibiotics, to find one or more which will be effective in treatment of the patient concerned. Sometimes administration of relatively huge doses of penicillin proves effective treatment before the degree of susceptibility of the infecting staphylococcus can be determined and such therapy, possibly combined with administration of a broad spectrum antibiotic, should be used at once if the illness is severe.

Streptomycin is effective against many gram negative bacilli which may, however, quickly acquire resistance to its action. It is also valuable in the treatment of tuberculosis, especially in the early florid phase of the disease. Its use in combination with para-aminosalicylic acid (PAS) and isoniazid had proven to be a wonderfully effective, but still far from satisfactory remedy. The tubercle bacilli are not exterminated. They may become resistant although the danger of resistance is reduced by giving the drugs in combination. The treatment must be continued for many months, and other measures must not be neglected. The use of these chemotherapeutic agents is, however, the greatest advance in treatment of tuberculous lesions to date. One wonders whether the incidence of tuberculosis infection will decrease with the decreasing mortality; it can be hoped for, perhaps expected, but it cannot as yet be predicted with confidence.

The introduction of the broad spectrum antibiotics, which are bacteriostatic only, offers a better means of treating infections

caused by many gram negative bacilli, some strains of staphylococci and some of the larger viruses. They are effective agents in typhoid fever (chloramphenicol especially) and brucellosis but have the disadvantage of allowing relapses to occur in many cases after apparent cure. The old problem of development of resistant strains also is always present.

One might mention the new chemotherapeutic agents used in treatment of malaria, amoebiasis, kala-azar, and others which offer a hope, in conjunction with adequate sanitation and other community measures, including relief of poverty, of controlling many tropical diseases[2].

One should not leave this subject without some discussion of the toxic effects of these specific remedies. All are potentially toxic but the ones mentioned are relatively safe in the usual effective dosage and fully justify the risk of use as specific agents. All may give rise to urticaria and other skin reactions in a small percentage of cases. They may cause severe and even fatal anaphylactoid reactions in very rare instances. The prolonged administration of streptomycin and dihydrostreptomycin, in the large doses initially used, often caused labyrinthine disturbances and deafness; but these unfavourable effects have been much less common with the smaller dosage now given. The broad spectrum antibiotics cause anorexia, nausea and sometimes diarrhoea in a small but important proportion of cases. Some relatively new remedies are too toxic for use except in highly specific indications when the outlook is bad and safe antibiotics ineffectual.

Newer antibiotics and other chemotherapeutic agents are being sought for and developed all the time and one may hope and expect that *safe* agents will be found which will be valuable in treatment of infections caused by those viruses and bacteria for which there is now no effective remedy. At present there is no agent useful in the treatment of poliomyelitis, measles, mumps and chickenpox, the common cold and most of the other diseases caused by viruses, including a number of respiratory and fungus diseases. The antibiotic therapy of infections caused by staphylococci, many gram negative bacilli, including typhoid and brucella, and tubercle bacilli is still unsatisfactory. One can look forward to better

measures from continued study, but the hope lies in the still uncertain future.

*Nutrition*

The recent great advances in treatment of infections were preceded by the great increase in the knowledge of specific factors in nutrition which have given vitamin preparations an exaggerated importance in ordinary therapy. Where there is no shortage of food the diet is likely to be adequate in all respects. In our countries there is little need for special vitamin therapy except in alcoholics who may suffer from thiamine and other deficiencies, in patients with mild mental derangements with obsessions about food and voluntary severe restriction of diet, temporarily in patients with severe postoperative complications requiring prolonged intravenous therapy, and in rare malabsorption syndromes such as steatorrhoea (sprue).

Undernutrition occurs chiefly in the poverty stricken people in some of the tropics, and also as a result of serious wasting diseases in all parts of the world, and relatively rarely as a self-inflicted disease like anorexia nervosa. It gives rise to weakness and apathy which are often enhanced by associated nervous influences. In affected children growth is slowed. If the diet is unbalanced there may also be specific vitamin deficiencies. In all cases there is an increase in extracellular water with shrinkage of cells and loss of protein and fat, and this goes on to gross oedema in a relatively small proportion of cases. There is an increased susceptibility to infections, including tuberculosis, which may become an important public health problem in wartime famine. The problem would virtually disappear were there adequate food supplies with free choice of different foods all over the world.

The nutritional problem which we face in North America is not one of scarcity but of prosperity and plenty leading in numerous instances to overweight and obesity. There is no time to discuss the important factors that affect the appetite other than to say that in most of us it is remarkably controlled so that our weight remains constant from month to month in spite of great short term changes in food intake and expenditure of energy and that the basic constitutional factors which seem to control it are modified

by physiological factors varying with the time of life, by emotional factors which depend at least in part on the soothing and pleasureable effects of food, and by habit and leisure. The important thing to recognize in therapy is that, whatever factors may have led to a surplus intake of calories over expenditure of energy, the resultant obesity can be corrected only by the self-imposition of a rigid dietary discipline. The physician may encourage and explain and direct but only the patient can perform, and when he does succeed he deserves great credit.

In his excellent studies of nutrition McCance[3] has pointed out that the emphasis placed on gain of weight in growing children, similar to the emphasis on gain of weight in production of fowl and live-stock, may be misplaced if judged from a long term view. He contends that even in the young overnutrition may be undesirable, although this is not immediately obvious. Speaking of conditions in England, he goes on to say that "we may be shortening the lives of the generation now growing up in this country by trying to make them grow faster with school meals and school milk." In the adult the effect of marked obesity appears to be obvious in the main, although not necessarily so for each individual. It aggravates hypertension and predisposes to diabetes. To quote McCance again, it may be "that forcing the metabolic process (through overnutrition) may turn out to be an aging factor in cells in many parts of the body . . . and it is certainly possible that the easiest way to add five years to man's expectation of life would be to prolong his years of growth on the calendar by controlled undernutrition and to maintain him on a low plane of nutrition for the rest of his life." There is little doubt that a broad mean level of nutrition from birth to death is better than extremes in either direction.

*The Reactive Diseases*

In recent years great interest has arisen in a group of diseases not caused by infection or disturbances in nutrition, nor by new growth, nor by degenerative processes but by a changed type of reaction on the part of the body. To call them reactive diseases is to use a poor, inadequate and quite unspecific term, perhaps with little justification for a distinctive meaning. For the time being, however, it is a convenient name applied to a heterogeneous

group of conditions, some of which may have little similarity in cause or effect. A list of some of the commoner reactive diseases is given below:

Rheumatic (fever) disease
Rheumatoid arthritis
Shoulder-hand syndrome

Lupus erythematosus
Scleroderma
Dermatomyositis
Periarteritis nodosa

Ulcerative colitis

Haemolytic anaemia
Some thrombopenic purpuras
Some agranulocytoses

Some definite allergic states

Asthma

Certain eye conditions such as iritis

It may be that this heterogeneous group of disorders lies somewhere between infectious diseases on the one hand and new growth on the other. All of them are characterized by a peculiar harmful reaction, often associated with a hypersensitivity, sometimes manifesting an antigen-antibody combination in which a serological reaction against some of the body's own tissue may play a definite role, as in some of the haemolytic anaemias and thrombocytopenic purpuras. Occasionally an external agent plays an obvious part in the development of the response which is then considered an allergic manifestation. Often there seems to be an underlying constitutional tendency to react in the special peculiar fashion, an inherent ability to suffer from this type of disease. There is great variability in the "natural" course of these disorders with a varying tendency to subside. In former days the chief therapy, apart from those in which an external allergen might be avoided, was pro-

longed rest. Now a new method of treatment has been introduced in ACTH and cortisone. This steroid therapy is often remarkably valuable, only too frequently disappointing, yet seldom without some effect. It commonly modifies the reaction and makes the patient more comfortable for a short time at least. The antigen-antibody union, if present, is not inhibited but its effect on the sensitized tissue cells may be modified or temporarily suppressed. If the reaction is likely to be a self-limited one, the symptoms may be controlled completely by the therapy while the reaction subsides.

At present the effect of ACTH-cortisone therapy in individual disorders of the group is of particular interest and it warrants a brief discussion.

It is of little value in rheumatic fever and its associated cardiac manifestations. Salicylates are usually just as effective. The progress of the valvular disease may be modified by prevention of streptococcal infections, but the peculiar process once started seems to be capable either of subsiding spontaneously or of persisting in varying degrees of activity, in some instances advancing relentlessly, in others lying almost dormant for many years.

In rheumatoid arthritis and allied disorders ACTH therapy may play an important role in conjunction with the usually more important measures of rest, prevention of deformity and reduction of muscle spasm. These disorders have a spontaneous but not invariable tendency to subside. If a small dose of 25 to 50 or even 75 milligrams of cortisone per day is effective in relief of symptoms it becomes an extremely valuable measure. In some low grade chronic cases a small dosage of cortisone gives almost complete relief. If larger amounts, 100 milligrams per day or more, are required to produce a material effect, as in approximately two-thirds of the cases, the patient is better without this type of therapy.

Of the more serious collagen diseases, lupus erythematosus responds best to ACTH and cortisone treatment. Because of the serious outlook of the disease large dosage of the drug is warranted and often the manifestations subside completely, but usually recur after periods varying up to several months if the dosage is greatly reduced or the drug discontinued. A number of our patients have been able to carry on in fairly good health on the daily ad-

ministration of 75 to 100 milligrams or more for a number of years. One always hopes for a prolonged or permanent spontaneous remission but to date few patients have been so fortunate, and in quite a number the disease has progressed to a fatal termination in spite of therapy. Polyarteritis, scleroderma and dermatomyositis do not respond nearly so favorably as does lupus erythematosus.

Ulcerative colitis, a peculiar reactive disease, may be helped greatly by this steroid therapy but, as with all other chronic diseases, it must not be used to the neglect of other measures known to exert a beneficial influence on the course of the disorder.

In haemolytic anaemias and purpuras there is often a spontaneous remission. Cortisone therapy may modify or control the manifestations until the remission appears. Unfortunately it may also fail to do so, and splenectomy may be resorted to with varying degrees of success. Agranulocytosis, often due to ingestion of a drug or other substance to which the patient has become sensitive, may respond well to cortisone therapy. In acute emergencies large dosage is warranted.

Allergic states like serum sickness and penicillin reactions commonly respond well to the treatment, although larger amounts than one may care to use may be required for relief of the symptoms.

The drugs are wonderfully valuable in many cases of asthma, especially when no external allergen can be demonstrated, small doses for short periods often being effective. It may be similarly helpful in a number of reactive eye diseases.

While discussing cortisone therapy it must be pointed out that this treatment also modifies the reaction of the body in acute infections, with temporary relief of symptoms. Unless an effective specific antibiotic is available, however, the ultimate result may be a dangerous spread of the disease. It is useful, though only temporarily so, in the nephrotic stages of nephritis. It may relieve pain and give a welcome sense of well being to patients dying with carcinoma. It should be pointed out also that cortisone therapy may be very valuable in the treatment of patients with that peculiar malabsorption syndrome commonly called idiopathic steatorrhoea or sprue.

The beneficial effects of cortisone have not proven to be as great as was hoped a few years ago except for its specific effect in replacement therapy of patients with adrenal cortical insufficiency. For this purpose it is a wonderfully good treatment now and may be improved by the newer preparations being introduced, some of which are more potent per milligram while others have more specific effects on electrolyte metabolism, and so on.

*New Growth*

Between the reactive diseases and chronic granulomatous infections on the one hand and the new growths on the other lie the chronic lymphocytic diseases such as lymphomas, leukaemias, Hodgkin's disease, among others, in which a temporary remission is often induced by ACTH-cortisone therapy. The therapy may be helpful in bringing a remission to a seriously ill person who may later be improved by radiation or other measures, but its long term effect is not great. This group of diseases may also be affected by various new chemotherapeutic agents and the effects obtained afford a basis for the hope that chemotherapeutic measures may be developed for the control of neoplasms in general. Unfortunately neoplastic diseases have exceedingly complicated enzyme systems like those of normal living cells and the problem of attacking them is not nearly so simple as in the case of infections where the antibiotic or other agent paralyzes enzyme systems in the minute infecting simple organisms, or in the case of the reactive diseases where special body reactions may be modified by a change in hormone-metabolic equilibrium.

That the present therapy of cancer is very unsatisfactory is indicated by the great and universal fear of the disease. The new growths that can be effectively treated by excision are those that grow and invade slowly and metastasize late if at all. The best example is rodent ulcer. There are a number of malignant diseases which, like some types of cancer of the thyroid, may metastasize widely yet have extremely slow growth — one such patient of ours was living and fairly well in spite of numerous obvious metastases twenty-six years after the first attempt to remove the growth. There is great variation in prognosis among individuals suffering from cancer of any particular organ or structure. For instance,

in some persons suffering from cancer of the breast, which has been recognized so early that the lump could scarcely be felt with certainty, immediate radical excision fails to prevent the early diffuse growth of metastases; in others, when the tumor may have been present and easily felt for a year or more, excision may not be followed by any recurrence. Tumors in certain locations such as the stomach or lung appear to offer a particularly bad prognosis, whereas those arising in the rectum or caecum are much less likely to recur after removal. That the inherent nature of the tumor and perhaps of the patient's reaction to it are most important factors in determining the value of excision or of other types of therapy becomes clear from experience, but at present it is impossible to measure these factors.

*Cardiovascular Diseases*

Little time need be spent in discussing the important cardiovascular diseases because a large part of your program is devoted to this subject.

The advances in surgical treatment of some types of congenital heart disease have placed great emphasis on the diagnosis as well as prevention, if possible, of these anomalies.

As judged from ordinary hospital experience, it would appear that rheumatic heart disease has a lower incidence than formerly. Whether this might be due to better treatment of haemolytic streptococcal infections, or their prevention in children is difficult to say. Surgical measures to increase the patency of the mitral valve have been gratifying in a number of cases but the problem of persisting rheumatic lesions is still important and unsolved.

The big problem in cardiovascular disease is, however, that of degenerative lesions. Factors that appear to affect them include the inherent constitution of the patient, obesity, hypertension and perhaps tension and strain. Current studies of atherosclerosis are difficult to interpret: the role of the cholesterol intake, the proportion of different sizes of the lipoprotein molecules in the plasma, the cholesterol blood levels and obesity. My own prejudice is to regard obesity as the greatest influence that may be modified and the inherent constitution of the patient as the most important single factor in the development of both atherosclerosis and hyper-

tension. It is relatively easy to have an individual patient reduce his weight but very difficult to do anything about it as a public health measure.

Hypertension offers a tremendous problem. It is difficult to define, and the word has different meanings for different people. There is as great a variation in the prognosis of different patients having persistently elevated systolic and diastolic blood pressure levels as there is between those with rodent ulcer and those with cancer of the stomach. In some persons hypertension runs a remarkably benign course lasting for several decades with little damage. In others, important tissue lesions follow vascular changes in brain, heart, kidneys and elsewhere at an early date, and patients with malignant hypertension usually have a rapid down-hill course. It is seldom possible to find an important aetiological factor which may be modified with good effect, such as unilateral renal lesions or coarctation of the aorta. Hypertension in most patients seems to be aggravated by anxiety, tension, driving excitement and obesity. Modification of these factors by the patient who sees his problem and wishes to cooperate under the encouraging supervision of his doctor is often wonderfully helpful. When obvious vascular and tissue lesions *begin* to appear, the restriction of salt and use of modern hypotensive drugs and, rarely, of surgical measures are sometimes useful. There is room for hope that careful study of the disease and of the present imperfect methods of therapy may lead to better measures in the future.

The treatment of actual passive congestive failure by carefully regulated rest, restriction of salt, mercurial and other diuretics and digitalis has given better results than used to be obtained. Many previously incapacitated patients have been able to work well, within their tolerance, for years. It is important not to restrict salt too rigidly; it is too bad to interfere unnecessarily with the patient's pleasure in eating; the prolonged severe restriction may lead to serious symptoms in very ill patients.

The treatment of patients with cardiac infarction is still very unsatisfactory. The use of anticoagulants appears to have reduced the morbidity and mortality from thrombo-embolic disorders but at best it is a clumsy and unsatisfactory therapy and one not without danger. Unfortunately the dread of the disease is so great that

many patients are unduly pessimistic and few realize how good their prognosis may be after recovery from the attack. Not appreciating that fear and anxiety in themselves may lead to weakness, fatigue and a sense of exhaustion, they attribute these symptoms, when present, to the cardiac lesion. The cause of these symptoms may be explained with great benefit and the patients should be encouraged to work within their tolerance while getting abundant rest. Many will live on in vigorous useful activity for years and years. Confidence and activity seem sometimes to increase their longevity.

*Miscellaneous Disorders*

There are many types of disorders which cannot be discussed for want of time, and also for fear of wearying you. I should like to have said something about gastrointestinal ulceration, in the aetiology of which the most important factor is the inherent constitutional predisposition. Aggravating factors, however, which include tension, excessive drive continued to undue fatigue, anxiety, lack of rest, ingestion of irritating foods and alcohol, and excessive use of tobacco, may be modified in successful treatment. They are, therefore, of first importance. I should have liked also to discuss the great advances in knowledge of endocrine control of the body and, in particular, the reciprocal control of function of the pituitary gland, gonads and thyroid and adrenal glands and their relation to the autonomic nervous control of the body. The great advances in endocrine preparation therapy — thyroid, insulin, cortisone, some pituitary and sex hormones, as well as others — are obvious on thinking about them. There is no time either to mention the advances that have occurred in knowledge and treatment of many haematological and neurological conditions. Great beginnings have been made and great problems remain. In ever so many types of disease and injury the value of modern surgical measures with their reduced morbidity and mortality need only be mentioned to be appreciated. Before concluding my remarks, however, and at the risk of wearying you, I should like to discuss briefly certain aspects of senescence and emotional disturbances and of the care of the patient in general.

*The Care of Aging Patients*

With advancing age there are many unfavorable changes. There is imperfect body regulation, the machinery runs less smoothly, symptoms arise from stresses and strains which the younger body would take with ease and these symptoms are often considered to be signs of serious disease and, accordingly, they give rise to needless worry. The reserve capacity is impaired; the body's storage batteries must be charged by resting more frequently and for longer periods. There is a general loss of tissue elasticity and a general shrinkage in size and number of cells. Wounds heal more slowly and recovery from illnesses is retarded. Important psychological changes also occur. Impressions are less striking and, for this reason, memory and ability to learn often seem to be impaired. The most unfortunate change, however, is a change in outlook. With a lack of looking forward may come anxiety, apprehension, fear and a sense of hopelessness which aggravates any symptoms already present and causes others. Fortunately mental deterioration, which so many people fear, comes relatively infrequently and usually late.

The important measures in treatment of aging people are to persuade them to continue in a life of physical and mental activity within their tolerance, to help them to understand their actual situation and to realize that most of their fears are groundless, and to give them clear advice about the desirable amount of rest and activity to be taken. All of them need more physical rest than was required in earlier years and the need increases with each decade. Rest is, however, not simply a matter of ceasing to toil or of lying down. It is a state of mind, a state of relaxation and tranquility which can be achieved in great degree only by persons who have interests and are active in outlook. Interest is perhaps the greatest physiological stimulus; it is necessary for normal body regulation and function; it has to do with appetite and tone and posture and movement. The physiological power of active mental processes is enormous. For the old and disabled, the psychoneurotic, and the bored, the greatest tonic is a genuine absorbing interest. The induced activity of mind and body allows of peaceful rest, and such rest can scarcely be obtained without it. The doctor can help the patient to become interested and to gain rest by explanation and

encouragement. Most important of all is a keen, kindly and persistently demonstrated feeling of interest in him and of faith and confidence in him and in his ability to do well. Supported by the doctor's help and care and encouragement the patient acquires interests and engages in increasing activities within his ability. But unless he understands his problem and cooperates actively, little is achieved. Without effort or striving and feeling for others life is vegetation. The patient is the one who must do something. But the desired physical and mental activity must have an aim and accomplishment; repetitive movements are of little use; hence the value of useful tasks and of games and of caring for others and learning to have the mind occupied with problems other than one's own.

There are a variety of other measures which may be necessary, depending on the patient's symptoms and state. Insistence on taking a well balanced diet is often important, especially for those living alone. Directions for care of the skin and the feet and many minor measures are commonly indicated. It is important, however, not to overtreat. If a measure is not definitely indicated it is contraindicated. It is particularly important to avoid the overuse of sedatives which may nullify efforts to increase the patient's physical and mental activity. If he is on a proper regimen and is not afraid of lying awake for frequent short periods they are not needed. Similarly, unnecessary investigation should be avoided — the most important investigation is to gain a clear understanding of the patient's conception of his own condition, his outlook and his habits so that needless fears and misapprehension can be allayed and a suitable regimen undertaken. Any lesions present, including the multiple degenerative processes that come with years, should be treated as would lesions of the same structures in younger people. It is important, however, for the older patient to understand that, while recovery from injury, infection or operation in the aged will be slow, improvement will continue for a very long time, commonly for months and years. It is a pity for them to suffer all the bodily ills that go with early discouragement and the belief that improvement has ceased and that only deterioration lies ahead. Such an outlook destroys interest and seriously interferes with physiological functions.

*Emotional Disturbances*

In the absence of serious lesions, the greatest enemy of health and efficiency throughout life is anxiety and fear and an imperfect or wrong attitude toward one's life and work. With this often comes the driving tension which makes people continue to work long after a healthy animal would have sense enough to lie down and rest unless driven by a need for life preservation. The most helpful physician is the one who can understand his patient's problems and can explain away unnecessary fears and help him to train himself, both mentally and physically, to live in a difficult world and often in environments which cannot be either avoided, escaped from or greatly altered. This is equally true in the care of patients with serious structural lesions. As Tolstoy pointed out, "they (the doctors) were of use, were needed, were indispensable in fact because they satisfied the eternal need of hope for relief, that need for sympathetic action that is felt in the presence of suffering." If the sympathy and personal support can be combined with skilful use of modern technical measures the disabilities of both serious structural diseases and functional disorders can be wonderfully alleviated.

*Importance of Critical Study of Therapeutic Measures*

In all ages the doctors who led advances in medicine were critical of accepted dogma and willing to study the effect of therapy by careful observation of the patient's response. Fernel began his medical work with a firm belief in astrology but found by observation that the illnesses of his patients were not affected by the stars. Modern medicine has its astrology too, its uncritical belief in the wizardry of science, its too ready acceptance of the newly advanced remedies on what appears superficially to be scientific evidence although often not supported by sound clinical observations made with a clear knowledge of the natural course of the disease and of the great effect of suggestion and faith in a new remedy. We may look down on the excessive blood-letting of our predecessors — Fernel was critical of excessive bleeding also — but we often give transfusions of blood needlessly and sometimes in harmful amounts. Much harm has been done by excessive administration of saline after operation and at other times, just because administration of saline when needed to relieve dehydra-

tion had been found to be wonderfully helpful. We are just escaping from a long period when useless removal of teeth and tonsils was widely practised in a vain hope of benefiting patients suffering from various rheumatic and other conditions. Every day we see instances of ridiculous overuse of costly preparations of vitamins and hormones in treatment of conditions that cannot be benefited by such therapy. It is common to find too much attention paid to tests that make an actual measurement of something about a patient and therefore appear to be scientific when a more scientific investigation would have been a detailed study of the patient and his symptoms and signs and the history of his earlier responses to various illnesses and strains.

If, like Fernel, we could all continue to learn by our experience even when our observations are in conflict with the established fashions of the day, if we could assess the results of new therapeutic measures and evaluate new tests thoroughly and without bias, more rapid advances would follow. If we can make use of the new diagnostic and therapeutic technical procedures without in any way diminishing our interest in our patients and our willingness to give them personal help and support when they need it, we shall see the present medical situation with all its imperfections improve greatly, if irregularly, and without loss of the wonderful heritage of the past.

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PRESIDENT MONTGOMERY — Thank you very much, Dr. Farquharson. I wonder if there are any questions.

DR. FRANK L. SPRINGER — Dr. Farquharson, I wonder if you could comment briefly concerning your opinion of the present status of an alleged cancer controlling substance reported by Dr. Ivy.

PRESIDENT MONTGOMERY — Are there any other questions? We will wait until we get them all together.

DR. FARQUHARSON — I cannot say anything about that from personal experience, but I have asked a great many people about it who have used it, and it is my opinion that it is of no value. I have seen in my time a great many cancer cures, and some of them have had remarkable effects on their patients, because even in the presence of cancer the effect of the psychic is wonderful. As Paracelsus said: "Be your faith true or false, it will work wonders."

We saw in Ontario the use of a cancer cure made from growth of a subtilis bacillus in broth cultures. It was reported as working wonders but, on careful observation, we could observe no beneficial effect at all. I think the same is true of Ivy's substance.

PRESIDENT MONTGOMERY — Thank you, Dr. Farquharson, and thank you very much for coming here to talk to us.

We are indeed honored to have as our second speaker this morning Dr. John H. Halliday, of Sydney, Australia. Dr. Halliday is Chief Medical Officer of The Australian Mutual Provident Society. He is also Honorary Physician in Cardiology at Royal Prince Alfred Hospital, Sydney, and Medical Director of the Life Insurance Medical Research Fund of Australia and New Zealand.

Dr. Halliday visited here previously in 1949, and is one of the two Australian members of the Association. We are very pleased to have our Australian colleague attend our meeting. He is well known as a raconteur extraordinary, a dedicated fisherman and an outstanding tennis player. It is our real pleasure now to hear Dr. Halliday on the subject of "The Differentiation and Assessment of Basal Systolic Murmurs."

# THE DIFFERENTIATION AND ASSESSMENT OF BASAL SYSTOLIC MURMURS

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For many years the significance of basal systolic murmurs has been a subject of continuous controversy.

Largely as the result of much brilliant technical investigation of the physiology of the circulation in health and disease, certain additional physical signs have been recognized which enable the physician of today to differentiate these murmurs more accurately. However, the origin and significance of certain murmurs still remain obscure, and their ultimate clarification will depend on the development of more precise diagnostic methods than those now available.

*Material*

A series of 1,000 patients referred to the Cardiac Department of the Royal Prince Alfred Hospital, Sydney, has been reviewed. These cases came from every section of the profession, and in many the murmur was discovered during a routine medical examination, or in the course of some unrelated illness.

Patients with central cyanosis (e.g., with veno-arterial shunts), patent ductus arteriosus, manifest aortic incompetence and mitral valve disease have been excluded. Further, those with essential hypertension, thyrotoxicosis, and severe anemia will not be discussed.

There remained 228 patients with basal systolic murmurs, who have been grouped as follows:

| | |
|---|---|
| TOTAL CASES REVIEWED | 1,000 |
| NUMBER WITH BASAL SYSTOLIC MURMURS | 228 |
| (i) Established Diagnosis | 185 |
| (ii) Indeterminate Diagnosis | 43 |

Functional Class of the 185 cases (New York Heart Association)

| | |
|---|---|
| Class 1 | 134 |
| Class 2 | 40 |
| Class 3 | 11 |
| ESTABLISHED DIAGNOSIS | 185 |
| A — Normal Heart | 48 |
| B — Left Heart Lesion | 52 |
| (i) Aortic stenosis | 22 |
| (ii) Ventricular septal defect | 20 |
| (iii) Coarctation of the aorta | 10 |
| C — Right Heart Lesion | 85 |
| (i) Pure pulmonary stenosis | 47 |
| (ii) Atrial septal defect | 38 |

For the sake of clarity, the murmurs have been defined as aortic, pulmonary, and left parasternal according to the site of maximum intensity, though in many the murmur was also audible elsewhere. At times the determination of the site of origin of a murmur is a matter of considerable difficulty.

First, the indeterminate group will be briefly discussed. The 43 cases included 29 in which there was unequivocal evidence of organic heart disease. In 7 of this 29, complicated or double lesions were suspected, and in 4 of these, this was confirmed by cardiac catheterisation and angiocardiography. The majority of the others in this 29 were children under ten years of age, whose investigations have not been completed. In the remaining 14 cases, the diagnosis rested between a normal heart and a mild atrial septal defect or pulmonary stenosis, and these cases will require further review and investigation.

*Innocent Basal Systolic Murmur*

The decision as to whether or not a murmur is innocent, is of primary importance. Concerning this, Sir James Mackenzie[1] wrote:

"To the human mind, sounds arising from obscure sources have always been a source of mystery, and the human imagination, when dealing with the mysterious, invariably associates it with something malign. This peculiar attitude is shown by the attitude of the profession towards murmurs and abnormal sounds of the heart. . . . It is true that some physicians recognize and acknowledge that some functional murmurs may be harmless, but when they attempt in their writings to deal with this problem, their words convey so confused an impression, that it is evident that they have but a hazy impression of the manner in which a harmless, functional murmur is to be distinguished from a murmur, which may be an indication of or associated with heart failure."

Murmurs of moderate loudness (more than grade 2 in the six grade classification of Freeman and Levine[2] (1933)) have long been viewed with suspicion. Recently Leatham[3] summed up as follows: "Improvements in the methods of diagnosis are leading to the view that there is always a cause for isolated murmurs of more than grade 2, if fairly constant from time to time, and not specially related to one phase of respiration. Such murmurs may indicate a slight valvular lesion, or if loudest in the pulmonary area, increased blood flow through the pulmonary artery. Increased blood flow through the aorta does not seem to cause a similar murmur unless there is some slight organic change in the valve or vessel as in aortic sclerosis."

In the 48 cases in which the murmur was regarded as innocent, it is of interest that in no instance was the murmur heard maximally in the aortic area, and this conforms with the view that isolated murmurs of grade 1 to 2 intensity heard best in the aortic area should be regarded with suspicion. As it happened, no such patients were seen in the series under discussion.

The features of the murmur in these 48 cases were as follows:

1. AGE — all under 40 years
2. FUNCTIONAL CLASS — all class 1
3. MURMUR
   - (i) Intensity — grade 1–2
   - (ii) Quality — soft

(iii) Maximum intensity — in pulmonary or left parasternal area

(iv) Variation with posture or respiration

4. ABSENCE OF OTHER PHYSICAL SIGNS OF C. V. DISEASE

5. NORMAL X-RAY AND ELECTROCARDIOGRAPHIC FINDINGS

Such murmurs are maximal about mid-systole, finishing before the second sound. The gap between the end of the systolic murmur and the second sound can often be appreciated clinically. This is in sharp contrast to the pansystolic murmur of ventricular septal defect and mitral incompetence. For obvious reasons this group has not been investigated exhaustively and may include a number of mild organic lesions.

It has been found that close attention to the following aspects of physical examination allows a more accurate differentiation of basal systolic murmurs, especially when these findings are correlated with x-ray and electrocardiographic evidence.

1. THE NATURE OF THE SECOND HEART SOUND

2. PALPATION OF THE PRAECORDIUM

(i) Presence or absence of thrill

(ii) Type of cardiac impulse

(iii) Right ventricular activity (3rd & 4th left intercostal space)

(iv) Pulmonary artery pulsation (2nd left intercostal space)

3. VASCULAR PULSATIONS IN NECK

4. PERIPHERAL ARTERIAL PULSES

5. X-RAY AND ELECTROCARDIOGRAPHIC FINDINGS

1. *The nature of the second heart sound.* In the pulmonary area this sound is normally split, the two components being most readily appreciated towards the end of inspiration and in the younger age groups. The first component is of aortic and the

second of pulmonary origin. Thus in pulmonary stenosis, unless this is of mild or moderate degree or infundibular in type, the second sound is single and abrupt, whereas in atrial septal defect the second sound is widely split. As pulmonary hypertension develops, the second sound becomes increasingly loud, from accentuation of the second or pulmonary element.

It is now recognized that the second sound in aortic stenosis may be of normal intensity even when the stenosis is of considerable degree.

2. *Palpation of the praecordium.*

(a) *Thrill.* The value of a thrill as a sign of organic heart disease has in recent years been seriously questioned. To regard the detection of a thrill as merely an academic curiosity is surely clinical heresy. The presence of a thrill is frequently overlooked from hurried or careless examination or from poor medical training. The absence of a thrill is an important differential point in distinguishing between an innocent left parasternal murmur and a ventricular septal defect, with which a thrill is almost always present.

(b) *The situation and type of cardiac impulse.* Palpation of the apex beat usually gives the best indication of heart size on physical examination. If forceful or heaving in type, a left-sided lesion is suggested, whereas in right-sided lesions the impulse may be reduced or tapping in quality, or impalpable.

(c) *Right ventricular activity.* The presence of right ventricular hypertrophy is indicated by a heaving, systolic thrust in the 3rd and 4th interspaces to the left of the sternal border. In severe right-sided lesions, the right ventricular impulse may extend to the left as far as the mid-clavicular line or even further and may be mistaken for a left ventricular impulse. This sign may be masked by a thick or fat chest wall.

(d) *Pulmonary artery pulsation.* The presence of an enlarged pulmonary artery is suggested by systolic pulsation, palpable in the 2nd left interspace. In this area, the accentuated second sound associated with advanced pulmonary hypertension may be appreciated as a palpable shock.

3. *Vascular pulsation in the neck.* Critical inspection of both arterial and venous cervical pulsations may provide significant evidence of altered haemodynamics. An example of this is the accentuated or giant 'a' wave visible in the jugular venous pulse, which is associated with the high right ventricular pressure met with in pulmonary or tricuspid stenosis and pulmonary hypertension. It should be pointed out that much time and patience is required to master this difficult but important clinical assessment.

4. *Peripheral arterial pulses.* The *pulsus tardus* of aortic stenosis is well known. More often neglected is the examination of femoral artery pulsation as to its volume and time relationship to the radial arterial pulse, so often illuminating in the presence of coarctation of the aorta.

5. *X-ray and Electrocardiographic findings.*

*X-rays.* Fluoroscopy and skiagrams each have an important role:

(a) *Abnormal size or contour of the heart and great vessels.* The recognition of slight enlargement of either ventricle remains a major difficulty. The earliest radiological sign of enlargement is frequently a change in contour.

A more specific diagnostic feature is the post-stenotic dilatation of the ascending aorta and pulmonary artery in stenotic lesions of the respective valves.

A slight prominence of the pulmonary artery with an associated pulmonary systolic murmur may occur in normal hearts. This is not an infrequent finding in the presence of sternal depression, of which six instances were encountered in the present series.

(b) *Vascularity of the lung fields.* With progressive increase in pulmonary blood flow, the lung fields assume a characteristic plethoric appearance, due to dilatation of the branches of the pulmonary artery. On fluoroscopy, these dilated branches are seen to pulsate vigorously. When pulmonary blood flow is reduced, as in moderate or severe pulmonary stenosis, the lung fields are ischaemic and have an unduly translucent

appearance. In the presence of advanced pulmonary hypertension this same translucency is apparent in the peripheral lung fields, which are in sharp contrast to the dilated and relatively immobile proximal branches of the pulmonary artery.

*Electrocardiographic findings.* The electrocardiogram is usually normal in the presence of mild lesions. In the severer types, left or right ventricular patterns emerge, and conduction defects of various types are encountered. In atrial septal defect the partial right bundle branch block pattern (in $V_1$) is a characteristic finding and this will be referred to later. Abnormally peaked "P" waves, of the so-called "P pulmonale" type, are met with in certain advanced right heart lesions.

Such then, in brief, are the most important clinical features which are of value in differentiating basal systolic murmurs.

Some of the lesions associated with pulmonary systolic murmurs may be complicated by pulmonary hypertension. The clinical recognition of this condition, if of more than mild degree, is now usually possible by integration of the features just discussed.

*PULMONARY HYPERTENSION*

Clinical signs of moderate and severe types:

Accentuated 'a' wave in jugular venous pulse

Right ventricle systolic thrust — 3rd and 4th left intercostal space

Palpable second sound — 2nd left intercostal space

Pulmonary artery pulsation — 2nd left intercostal space

Second heart sound pulmonary area — very loud with or without Graham Steell — Diastolic Murmur

X-rays — pulmonary artery prominence with ischaemic peripheral lung fields

Electrocardiogram — right ventricular patterns

To these should be added a right auricular gallop rhythm audible at the base of the sternum, and the recently described pulmonary systolic ejection sound, a high-pitched clicking sound occurring immediately following the first sound and heard best in expira-

tion. This clicking sound is audible in various conditions associated with enlargement of the pulmonary artery.

Turning now to individual lesions in this series — pulmonary stenosis and atrial septal defect will be reviewed as right heart types, and aortic stenosis as a left heart lesion.

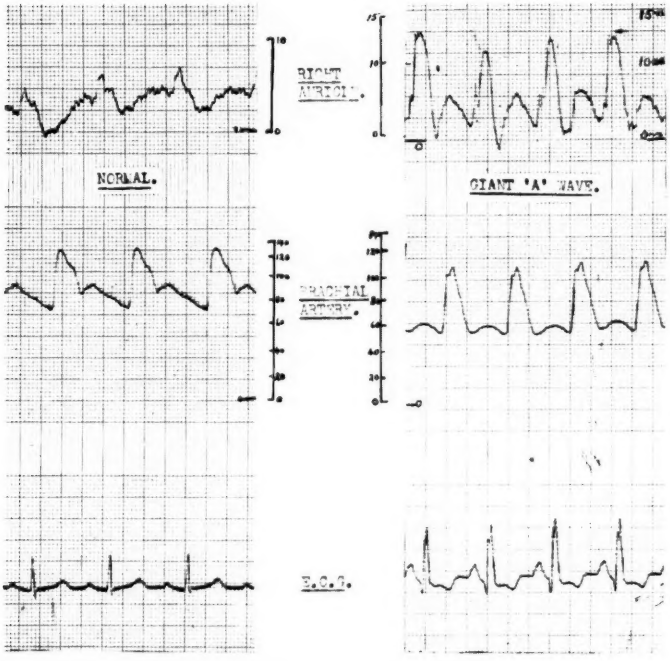


Fig. 1. Giant 'a' wave in pulmonary stenosis obtained during right heart catherization.

*Pulmonary Stenosis* — With normal aortic root. The great majority were under 20 years of age, and over half were asymptomatic. The systolic murmur in this condition is usually harsh and of grade 3 or more intensity, but in the mild and very severe types may be grade 2 or less. A thrill is almost a constant finding, though

## *PULMONARY STENOSIS*

47 cases

| Males 23 | | Females 24 | |
|---|---|---|---|
| Ages | | Functional Class | |
| 0 – 20 | 38 | Class 1 | 28 |
| 21 – 40 | 6 | Class 2 | 14 |
| 41 – 60 | 3 | Class 3 | 5 |
| Murmur | | Thrill | |
| Grade 1 – 2 | 13 | Present | 45 |
| Grade 3 or more | 26 | Not detected | 2 |

Second heart sound — pulmonary area

| | |
|---|---|
| Split | 21 |
| Single | 26 |
| Diminished | 9 |
| Loud | 4 |

in four severe cases operated on, not in the present series, no thrill was detected on repeated examination. With mild and moderate degrees of the common valvular type of stenosis, or in the infundibular type, the second sound may be split, but in the majority of the present series the second sound was single. An accentuated 'a' wave was present in 16 cases, in five of which it was of the giant type. Palpation over the right ventricular outflow tract revealed evidence of right ventricular activity in 36 cases. The presence of a definite systolic thrust in the 3rd and 4th interspaces as mentioned earlier denotes right ventricular hypertrophy, but evidence of lesser degrees of right ventricular activity must be interpreted with caution, particularly in an overacting heart with a thin chest wall, and in these instances the electrocardiogram is a valuable check. This sign of right ventricular hypertrophy is not present in the less common infundibular type of pulmonary stenosis.

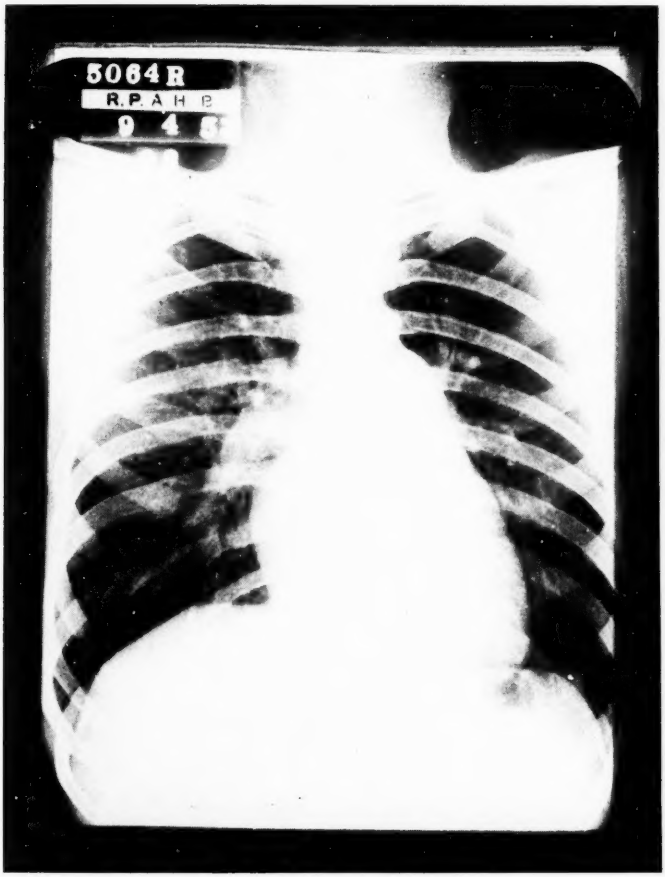


Fig. 2. Gross dilatation of pulmonary artery and proximal branches with translucent peripheral lung fields in advanced pulmonary hypertension.

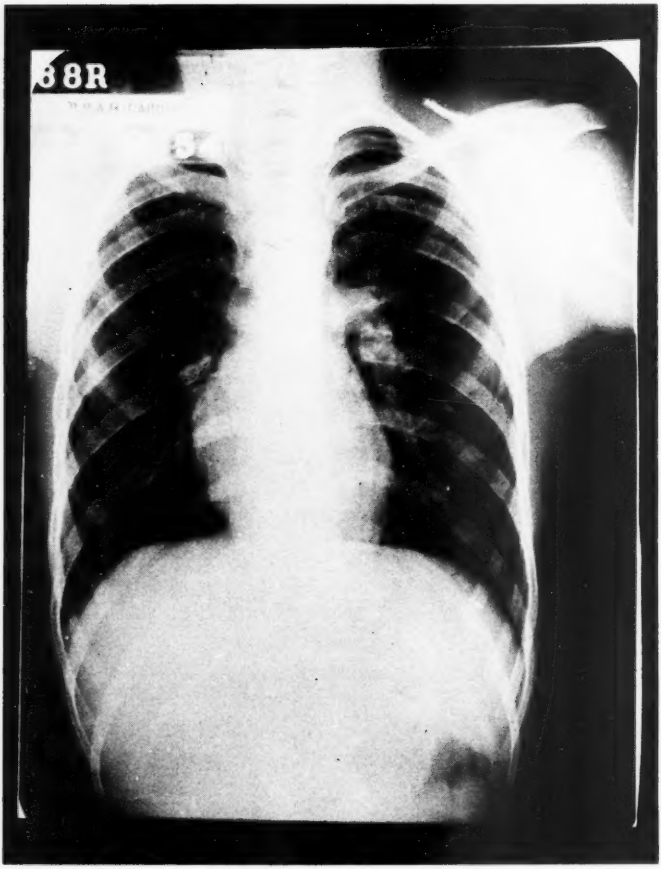


Fig. 3. Pulmonary stenosis–
(a) x-ray showing poststenotic dilatation of pulmonary artery.

*PULMONARY STENOSIS (Continued)*

X-ray findings

Heart size
- Normal ..... 26
- Enlarged ..... 21

Pulmonary artery enlargement ..... 32

Pulmonary artery pulsation ..... 10

Lung fields
- Normal ..... 34
- Ischaemic ..... 13

Electrocardiogram

- Normal ..... 18
- Abnormal P waves ..... 6
- Right ventricular preponderance ..... 21
- Right bundle branch block 8

Radiologically the heart was of normal size in 26, but the main pulmonary artery was prominent in 32, in 10 of which mild intrinsic pulsation of the artery was observed on fluoroscopy. In 13 cases the peripheral lung fields appeared ischaemic. In the electrocardiogram varying degrees of right ventricular preponderance were present in all but the mildest types. In the severe group, T wave inversion in the praecordial leads extended to the left as far as $V_5$. Abnormally peaked symmetrical P waves were present in six severe cases, on all of which patients operation has been performed.

From this data three classes of pulmonary stenosis emerge and may be described as follows:

1. *Mild.* Such patients are acyanotic and symptom-free and able to undertake heavy manual work. The only significant abnormal physical signs are a high pulmonary systolic thrill and murmur. A normal left ventricular cardiac impulse is present. Radiologically the heart size and lung fields are normal, but in the great majority dilatation of the main pulmonary artery is seen. The electrocardiogram is normal. Cardiac catheterization reveals a normal pulmonary artery pressure, and a right ventricular systolic pressure between 20 and 50 mm. Hg. The cardiac output is normal.

2. *Moderate.* These patients are still symptom-free with normal jugular venous and peripheral pulses. The cardiac impulse

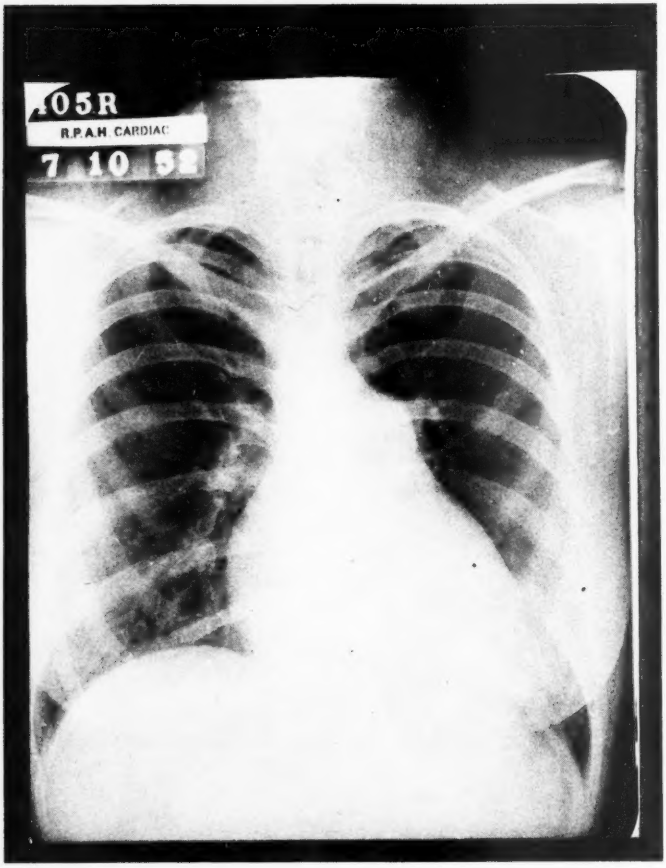


Fig. 3. Pulmonary stenosis–

(b) severe type, x-ray showing gross enlargement of right heart and pulmonary artery and translucent lung fields.

can only be felt with difficulty if at all, whereas some degree of increased right ventricular activity is now apparent. The pulmonary systolic thrill and murmur are obvious and the second sound is well split, though the second or pulmonary element is soft. Radiologically, some prominence of the right heart is seen in addition to the dilated pulmonary artery, and the lung fields may appear somewhat translucent. The electrocardiogram shows slight or moderate P pulmonale and right ventricular preponderance. On catheterization the pulmonary artery pressure may be slightly reduced, the right ventricular pressure is between 50 and 100 mm. Hg., and though the cardiac output is normal at rest, it is somewhat limited on effort.

3. *Severe.* Symptoms attributable to low cardiac output are now present — dyspnoea, fatigue, dizziness on effort, occasionally angina pectoris, and congestive cardiac failure may develop. Peripheral cyanosis is common. The face may have a bloated appearance. The peripheral pulse is small and a giant 'a' wave is present in the jugular venous pulse. In the valvular type a conspicuous

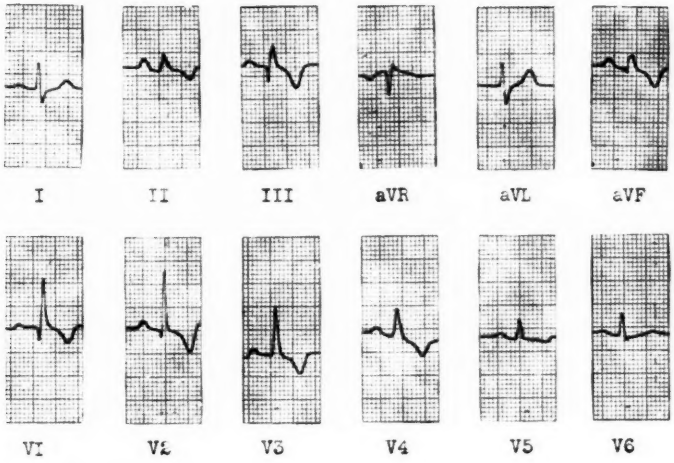


Fig. 3. Pulmonary stenosis–

(c) electrocardiogram showing pattern of right ventricular strain with T wave inversion in praecordial leads from V1 to V5.

right ventricular heave may extend from the left sternal border to the mid-clavicular line. A right auricular gallop rhythm is present. The second sound is usually single. X-rays show considerable right heart enlargement, dilated pulmonary artery and ischaemic lung fields. The pulmonary artery pressure is low and the right ventricular pressure is between 100 and 200 mm. Hg. The cardiac output is low and relatively fixed.

### *ATRIAL SEPTAL DEFECT*

38 cases

| Males 17 | | Females 21 | |
|---|---|---|---|
| Ages | | Functional Class | |
| 0–20 | 17 | Class 1 | 20 |
| 21–40 | 17 | Class 2 | 13 |
| 41–60 | 4 | Class 3 | 5 |
| Murmur | | Thrill | |
| Grade 1–2 | 24 | Present | 9 |
| Grade 3 | 11 | Not detected | 28 |
| Not recorded | 3 | Not recorded | 1 |

Second heart sound — pulmonary area

| | |
|---|---|
| Widely split | 27 |
| Split | 11 |
| Accentuated | 6 |

*Atrial septal defect.* It will be noted that 21 of this group were over the age of 20 but only four were over 40 years of age. Twenty were asymptomatic, though cardiac enlargement was present in 29. This condition is frequently overlooked, largely due to the fact that the systolic murmur, the only obvious physical sign in many instances, is not usually more than grade 2 and often soft, and so dismissed as being innocent. In 24 of the 38, it was of this order. Suspicion should be aroused by the presence of a widely split second sound, hyperdynamic right ventricular activity and

pulmonary artery pulsation, and a reduced or impalpable left ventricular apical impulse. A faint blowing diastolic murmur was present in the pulmonary area in 16 cases in this series.

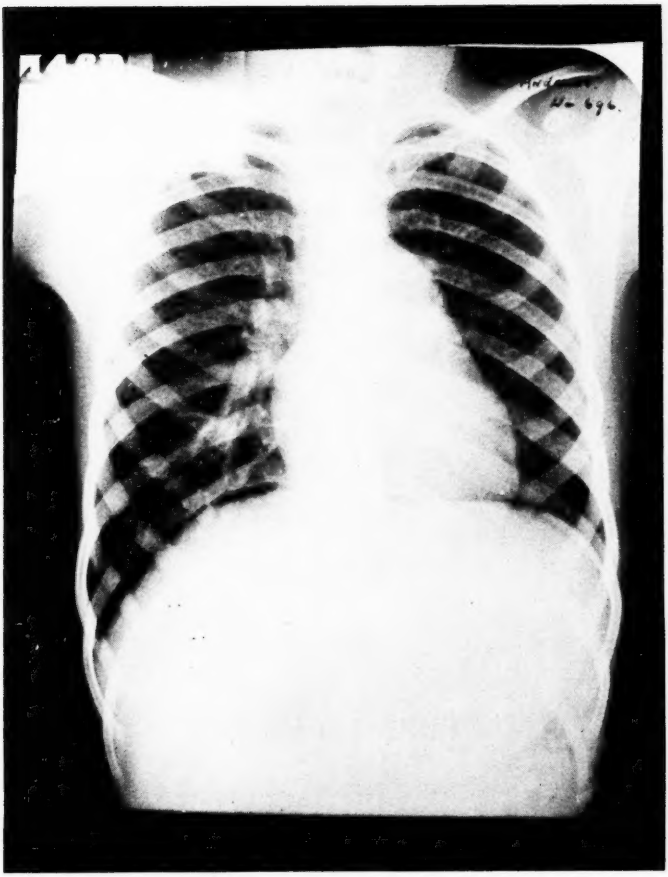

Fig. 4. Atrial septal defect–
(a) moderate shunt, x-ray showing dilated pulmonary artery and branches with slight plethora of lung fields.

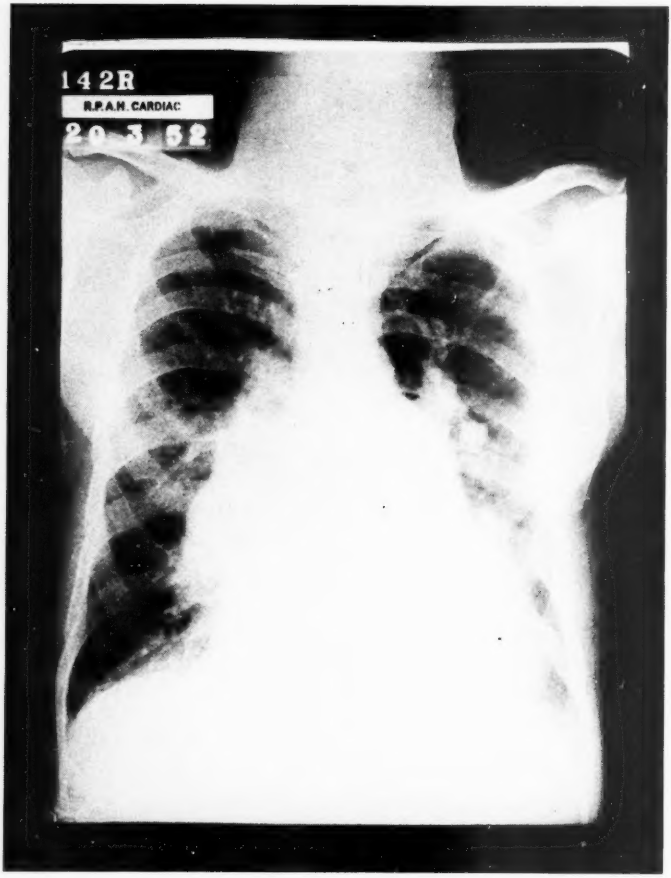


Fig. 4. Atrial septal defect–
(b) gross shunt, x-ray showing great enlargement of right ventrical, pulmonary artery and its branches.

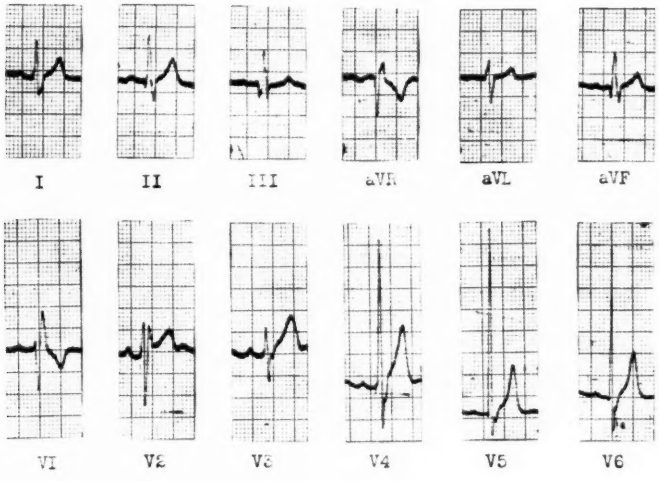


Fig. 4. Atrial septal defect–
(c) electrocardiogram showing partial right bundle branch block in leads V1 and V2.

## *ATRIAL SEPTAL DEFECT (Continued)*

| X-ray findings | | Electrocardiogram | |
|---|---|---|---|
| Heart size | | Normal | 0 |
| Normal | 9 | Right ventricular preponderance | 1 |
| Enlarged | 29 | Partial or complete right bundle branch block | 37 |
| Pulmonary artery enlargement | 34 | | |
| Pulmonary artery pulsation | 26/32 | | |
| Lung fields | | | |
| Normal | 2 | | |
| Plethoric | 31 | | |
| Not recorded | 5 | | |

Additional evidence is usually disclosed by the radiological appearances of a dilated pulmonary artery, plethoric lung fields and intrinsic pulsation of the branches of the pulmonary artery. These x-ray appearances were present in over 30 of the 38 cases. A

partial right bundle branch block pattern in Lead $V_1$ was observed in all but one of the present series. This is in conformity with Wood's view[4] that the clinical diagnosis of atrial septal defect is almost untenable in the absence of this electrocardiographic pattern. It will be of interest to observe whether this view is confirmed by further experience.

*Aortic stenosis.* Though in eight of this group a soft aortic diastolic murmur was found, no evidence of aortic incompetence was present either in the peripheral circulation or blood pressure. Thus these cases conform to the generally accepted definition of "pure" aortic stenosis.

*AORTIC STENOSIS*

22 cases

Males 18 Females 4

Functional Class

| | |
|---|---|
| Class 1 | 18 |
| Class 2 | 3 |
| Class 3 | 1 |

| Murmur | | Thrill | |
|---|---|---|---|
| Grade 2 | 1 | Present | 17 |
| Grade 3 or more | 17 | Not detected | 5 |
| Not recorded | 4 | | |

Second heart sound — aortic area

| | |
|---|---|
| Normal or increased | 10 |
| Diminished | 6 |
| Not specified | 6 |

The great majority were males. Two features were of particular interest — the first, the age of discovery of the murmur (50 per cent before the age of 10 years), and the second, the complete absence of any rheumatic history. Kiloh[5] who reviewed a series of 27 cases of this type in 1950 had similar findings. It

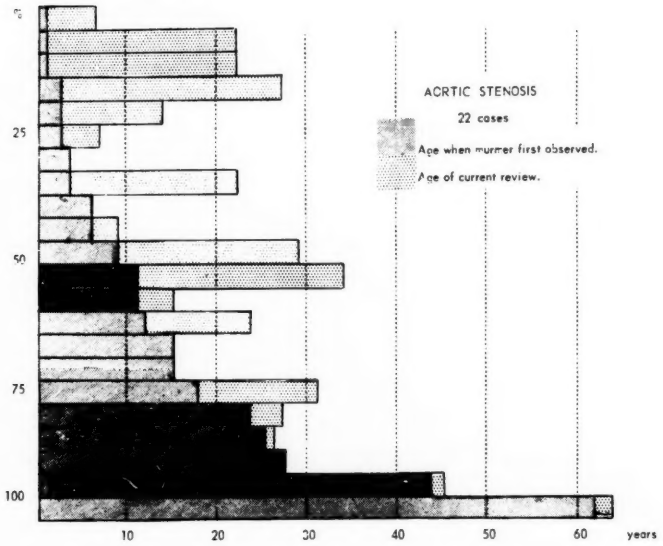


Fig. 5. Ages at which systolic murmur was first recorded.

is generally agreed that rheumatic involvement of the aortic valve is usually associated with manifest aortic incompetence[6, 7], whatever the degree of stenosis. The etiology of this condition does not therefore appear to be rheumatic and is generally regarded as being congenital[8]. The suggestion that this condition may emerge in the latter half of life as the calcific degenerative type of aortic stenosis is an intriguing one. Eighteen of the group were asymptomatic, though the heart was of normal size in only 11. While the harsh systolic murmur is usually heard maximally in the second right intercostal space, where the accompanying thrill is also best elicited, the murmur at times may be of equal intensity in the mid-sternal region, and the differentiation from ventricular septal defect may not be so easy. The characteristic diamond shape of the aortic murmur as seen in the phonocardiogram, mid-systolic in time and terminating before the second sound, is diagnostic in such instances. The aortic murmur may also be well heard at the apex and may be mistaken for the murmur of mitral regurgitation. The second heart sound was normal in at least half

the cases. Brown's[9] view that the retention of a normal second sound is of value in differentiating between valvular and subaortic types of congenital aortic stenosis is now seriously questioned and it is doubtful whether the clinical differentiation of these two lesions is possible. Angiocardiography may possibly be of assistance in this problem.

*AORTIC STENOSIS (Continued)*

X-ray findings

| | |
|---|---|
| Heart size | |
| Normal | 11 |
| Enlarged | 11 |
| Dilated ascending aorta | 11 |
| Calcified aortic valve | 1 |

Electrocardiogram

| | |
|---|---|
| Normal | 13 |
| Left ventricular preponderance | 8 |
| Left bundle branch block | 1 |

A dilated pulsating ascending aorta was present radiologically in half of the cases. The electrocardiogram was normal in 13, and in the remainder a left ventricular pattern, frequently with a vertical electrical axis, was present.

In certain obscure basal systolic murmurs, a precise diagnosis may be established by the use of more elaborate diagnostic methods, such as cardiac catheterization, angiocardiography and phonocardiography.

In common with apical systolic murmurs, the louder the basal murmur, the more likely is it to be a sign of organic heart disease, but it is emphasized that a number of basal systolic murmurs of grade 2 or less may be the presenting sign of an organic lesion. On the other hand, of the 228 cases under discussion, all referred as cases of suspected heart disease, 48 were regarded as having innocent murmurs, and with no such prior selection the proportion of such murmurs would be far greater.

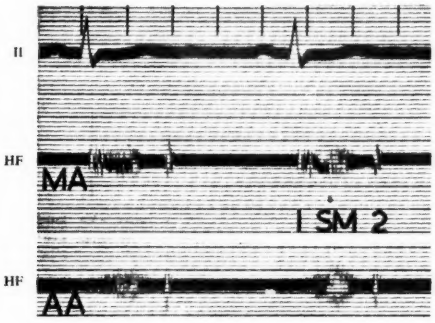


Fig. 6. Phonocardiogram of aortic stenosis.* The systolic murmur starts soon after the first sound, rises to a peak about mid-systole, and diminishes before the second sound. The murmur has the same shape in synchronous high frequency records (HF) from the mitral area (MA) and aortic area (AA). The time interval in this and subsequent records is 1/5 sec.

Thus, despite the uncertainties and difficulties that remain, it is believed that by appropriate integration of the physical signs, x-ray and electrocardiographic evidence which have been discussed, the interpretation of basal systolic murmurs should be less hazy and inaccurate than it sometimes is, and that if Sir James Mackenzie were alive today, he would agree that some progress had been made.

Rarely, however, should a systolic murmur, as a lone physical sign, be the sole basis for the consideration of the presence or absence of heart disease.

## *ASSESSMENT*

It has recently been said — "In underwriting, accuracy is the first resolve of the uninitiated, but broad consistency is the ultimate resort of the experienced."

Thus it is realized that the clinical approach to the problem of basal systolic murmurs just outlined demands an amount of reliable information which, for various reasons, is not usually available either in ordinary or special medical reports.

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*Reproduced by courtesy of the Editor, British Medical Bulletin, (Leatham, A.: Brit. M. Bull., 8.333, 1952).

Further difficulties arise from the fact that there is a wide variation in severity of these lesions from case to case, and that the life history of individuals with these lesions has not as yet been adequately studied.

Two other factors should also be mentioned. The first concerns subacute bacterial endocarditis. Growing experience suggests that while this infection can now as a rule be controlled, the damage to the valve cusps and myocardium is usually so great by the time the condition is recognized and treatment begun that this complication remains a most lethal one. The emergence of resistant strains of organisms is another serious aspect. The second factor is that of corrective surgery. Surgical measures for a number of these lesions have already been established, and with the probable availability of a bloodless field in the near future, it seems likely that an increasing number of these patients will undergo operation. Most of these procedures have a significant mortality rate, and in many cases the ultimate benefit to life expectancy is largely unknown.

With these points in mind, for assessment purposes, basal systolic murmurs may be divided into three groups:

1. Innocent murmurs
2. Murmurs regarded as organic but where no definitive diagnosis can be established
3. Murmurs associated with determined types of organic heart disease

1. *Innocent murmurs.* The criteria given for regarding a murmur as innocent will doubtless allow the inclusion of some very mild organic lesions, but in my opinion the acceptance of this group at standard rates will not involve significant extra mortality.

When the information submitted is incomplete or raises doubt in the underwriter's mind, the risk should be regarded as substandard.

2. *Murmurs regarded as organic* but occuring as an isolated finding. This is a difficult substandard group and will require detailed investigation in the manner outlined earlier in this paper. Where, despite such investigation, the murmur remains as an isolated finding, as in the aortic systolic murmur attributed to aortic

sclerosis, the intensity and site of the murmur should form the basis for assessment.

3. *Murmurs associated with defined organic lesions.* Important factors in this group are:

(i) Age of applicant
(ii) Functional class
(iii) Type of lesion
(iv) Radiological and electrocardiographic findings

(i) *Age of applicant.* This is of particular significance in applicants under 30 years of age. For example, in the presence of septal defects, individuals may remain asymptomatic until the fourth decade, when symptoms of cardiac insufficiency and failure develop and death may occur within relatively few years. On the other hand, an individual with aortic stenosis, who presents himself between the ages of 15 and 30 asymptomatic and with a normal-sized heart, may have a long life expectancy and only develop cardiac symptoms in the sixth or seventh decade. Individuals with moderate or severe pulmonary stenosis have a mortality rate which renders them unassurable in many companies but the outlook for mild cases appears to be similar to that for mild aortic stenosis.

(ii) *Functional class.* The interpretation of the commonest symptom, dyspnoea, remains a matter of constant difficulty, and this is particularly so in life assurance medical reports. The presence of cardiac enlargement, though compatible with unimpaired cardiac efficiency, should outweigh any actual or apparent lack of symptoms.

(iii) *Type of lesion.* Allusion has already been made to this when discussing the age of the applicant. When possible the mildness or severity should be assessed in relation to evidence of altered haemodynamics, heart size and electrocardiographic changes, as illustrated in the discussion of pulmonary stenosis. In right heart lesions the radiological evidence of cardiac enlargement, the degree of pulmonary artery dilatation, the presence of plethoric or ischaemic lung fields, and electrocardiographic patterns of right ventricular preponderance are the important positive findings. In left-sided lesions, cardiac enlargement and an electro-

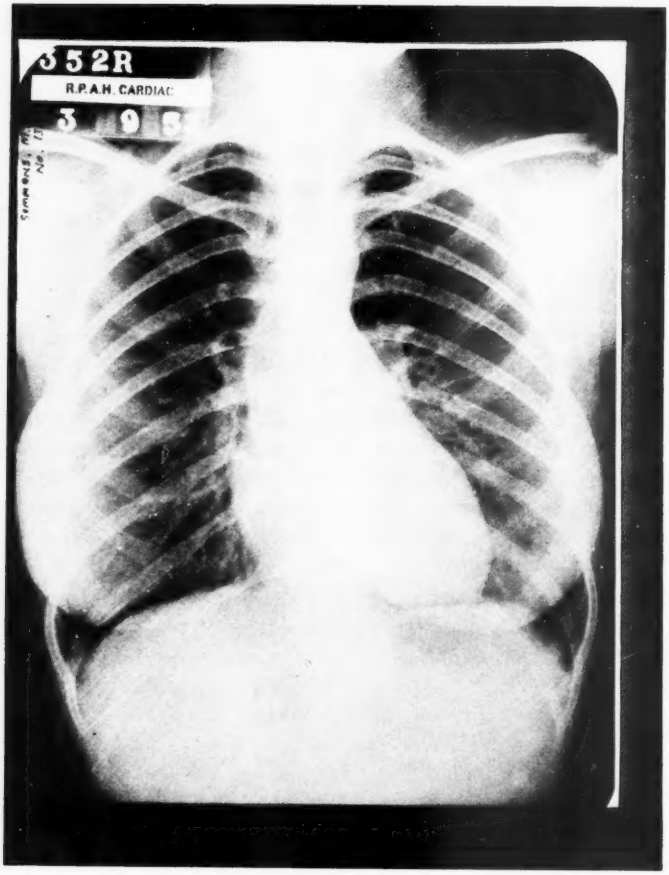


Fig. 7. Aortic stenosis, x-ray showing dilatation of ascending aorta.

cardiogram of left ventricular preponderance are of most significance, as they may be present in a symptom-free individual.

(iv) *Radiological and electrocardiographic findings.* When these are both normal, the lesion is usually mild, whereas increasingly abnormal findings occur with the grosser defects.

It is therefore suggested —

1. That, with reasonable care, innocent basal murmurs can be satisfactorily differentiated and accepted at standard rates.

2. That the cause of the majority of organic murmurs can be established and that, with careful evaluation, a significant proportion of these cases are assurable as substandard risks.

3. That there remains the necessity for a long-range study of the natural history of the various lesions associated with basal systolic murmurs to determine more accurately the appropriate ratings which should be applied.

.....

In conclusion, may I once again thank you for the great honour you have shown me in asking me to address you. I can only hope that, despite the imbalance between the clinical and underwriting aspects of my remarks, some of the points raised have been of sufficient interest to justify the time taken up this morning.

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PRESIDENT MONTGOMERY — Thank you very much, Dr. Halliday. I am sure there will be some discussion.

DR. HENRY B. KIRKLAND — As one who has had the opportunity to visit Dr. Halliday's native habitat, I would just like to have this opportunity publicly to commend him, as I have privately in the past few weeks, for what I think is an excellent presentation. It is one which we can take to heart in pointing up the necessity of paying more attention to the analytical side of physical diagnosis than we have been willing to do. Our impairment studies are all well and good, but nevertheless they are not sufficiently broken down, and I think John Halliday has done a remarkable job in giving us this thought-provoking presentation. It should lead us, I think, along more accurate lines in our physical evaluation of this difficult subject.

PRESIDENT MONTGOMERY — Thank you, Dr. Kirkland.

DR. ALFRED A. WILLANDER — In the differentiation of these basal systolic murmurs of less than grade 2 intensity, is the exercise tolerance test of any significance?

DR. HALLIDAY — Well, after all, these systolic murmurs at the base are usually ejection murmurs. Therefore, with exercise increased blood flow produces more turbulence, and the murmur becomes louder. Is that what you mean?

DR. WILLANDER — Yes.

DR. HALLIDAY — Yes, you can do that.

PRESIDENT MONTGOMERY — Any other questions?

DR. RICHARD M. NAY — I should like to ask Dr. Halliday if he would like to continue on the diagnosis of ventricular septal defects, and give a brief resumé of the age group and the criteria that he considers necessary for that diagnosis.

DR. HALLIDAY — Well, I am sure I have spoken over my time already, and I think it would be very improper for me to attempt in a few words to go into the differential aspects as to diagnosis of ventricular septal defects. Suffice it to say that in the nonhypertensive type it is essentially a left-to-right lesion.

I suppose if one had to pin it down to two things or three things clinically, this being similarly a left sided lesion, here is usually a forceful left ventricular impulse, secondly, the characteristic

thrill and murmur are in the third and fourth left intercostal space and thirdly, there is a widely split second sound in the pulmonary area.

PRESIDENT MONTGOMERY — Thank you very much. Are there any other questions now?

DR. W. J. MCCRISTAL — It might seem somewhat indelicate of me to amplify Dr. Kirkland's remarks as to the standard of Dr. Halliday's presentation, but the standard of excellence of his presentations is quite familiar to us in Australia.

Our experience in Australia is notably yours, in the sense that we go largely by intuition in the case of these systolic murmurs, and we only regard the underwriting of them as — well, no greater or less than the source. However, the question has been raised today, and I may not have heard some comments — I may have missed his observations — but the transmission of these murmurs, might he tell us something about that? Has he been able to examine into that direction, as to the significance of the transmission?

DR. HALLIDAY — Dr. McCristal, I think it depends on where you stand as to how much you are a devotee of Dr. Levine. He believes largely that the transmission of murmurs depends upon one function; that is, their intensity. So, arbitrarily a grade 2 murmur is local, whereas with grade 3 and 4 murmurs there is an increasing area of transmission.

I think it would be a bit difficult to go into the various theories and ideas of certain basal murmurs being conducted up or widely over the praecordium and the mitral murmurs through to the back, but I think the degree of transmission is largely a function of intensity.

PRESIDENT MONTGOMERY — Any further questions? We are indebted to our two speakers this morning for two very good papers indeed. Our next speaker on the scientific program is Dr. John Gemmell, Medical Director of the Monarch Life Assurance Company of Winnipeg, Canada. John Gemmell is a westerner born in Winnipeg and he graduated from the Medical School, University of Manitoba, in 1941. Shortly after graduation he joined the Royal Canadian Army Medical Corps and spent four

years in service, being a medical specialist in army hospitals in England, Italy and Germany. He also found time to attend the British Post-Graduate School, London, and obtained membership in the Royal College of Physicians, London, in 1946. Since then he has worked in Winnipeg as consultant to the Deer Lodge Veterans Hospital, Assistant Professor of Medicine of the University of Manitoba and Assistant Physician, Winnipeg General Hospital. He is especially interested in diseases of the thyroid and will speak to us today on "Radioactive Isotopes and Insurability."

We are glad to hear from Dr. John Gemmell.

# RADIOACTIVE ISOTOPES AND INSURABILITY

JOHN P. GEMMELL, M. D., M.R.C.P. (Lond.), F.R.C.P.(C)
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*The Monarch Life Assurance Company,*
*Winnipeg, Manitoba*

Twenty years ago, the successful artificial induction of radioactivity in an element was announced and eight years later the radioactive isotope of iodine was first used in the treatment of hyperthyroidism. The atomic reactors, developed in World War II, made radioactive isotopes readily available with resultant great expansion of this previously limited field. The chemical behavior of a radioactive isotope is identical to the non-radioactive stable element but these unstable isotopes emit radiation that can be detected and measured. This radioactive label is invaluable in tracing the metabolism of various elements and compounds in biological material, human and otherwise. Also, advantage has been taken of the radiation they emit to diagnose and treat certain diseases. Unfortunately, this unique property of radioactivity produces hazards to health that are significant in the assessment of risks among insuring individuals who have received these useful by-products of the atomic bomb.

The hazards will be discussed before considering the applications of radioactive isotopes to medicine. This is in accord with Hippocrates' dictum of "First, do no harm." While this paper deals with internally administered radioactive isotopes the bulk of our knowledge of the action of radiation is derived from experience with external radiation.

Radiation hazards might be divided into immediate effects and late effects. The immediate effects of radiation are not of such concern to life insurance medical examiners as the late effects of radiation, but passing attention will be devoted to this aspect. As physicians, we are all familiar with radiation sickness, characterized by nausea and vomiting, that occurs from the use of therapeutic x-rays. The introduction of the atomic weapon has forced attention on the effects of acute massive radiation with the pro-

duction of a complex group of symptoms known as the acute radiation syndrome with a high fatality rate. These changes may result from both external radiation and from internally ingested radioactive isotopes. The hematologic effects of radiation are a major hazard, and it is perhaps of interest to see what happens when a deliberate overdose of an internally administered radioactive isotope is given to a patient with advanced malignant disease. Radioactive phosphorus tends to localize in rapidly growing tissues, such as malignant metastases, but also unfortunately tends to accumulate in bone and in the bone marrow, so that a major effect is on the marrow cells. The administration of two doses of 10 mc. and 8 mc. of radioactive phosphorus resulted in profound leukopenia, thrombocytopenia and finally anemia. The clinical course was marked by an extensive haemorrhage, necessitating repeated transfusions. After a period of about 10 weeks there was evidence of recovery before the patient succumbed to the original disease.

The late effects of radiation are of more consequence to the life insurance medical examiner as he must assess the risk of a person who has been exposed to radiation. The early history of radiology is studded with tragic accidents from the use or misuse of radiation. In 1895 Roentgen announced the discovery of x-rays. By 1896, x-ray dermatitis of the hands had been described, and by 1902, a scant 7 years from the announcement of the discovery, the first case of cancer developing in a chronic x-ray ulcer was reported. Since then, many examples of malignancy developing in an area of radiation damage have occurred. This late production of malignancy is the most important ill effect in the evaluation of the life insurance risk. By 1911, late carcinoma in areas subjected to x-ray exposure had been well described and in this description the latent period before the ultimate production of carcinoma of the skin was emphasized. In common with other carcinogenic agents, radiation will cause malignancy more certainly if chronic exposure has occurred. However, carcinogenesis may occur in the absence of the primary stimulus providing the initial effect has been severe enough to produce damage to the tissues. However, these changes were the result of external radiation, and while they apply to internal radiation equally well, direct evidence of the ill effects of internally administered isotopes was shown by the late

results of radium and mesothorium poisoning in dial painters. Martland in his classical studies on the luminous dial painters, who had ingested sufficient quantities of radioactive elements, described two types of cases with ill effects. The first of these were the early cases developing within 5 years of exposure which were characterized by the presence of jaw necrosis and anemia. The late cases developed radiation osteitis, mild anemia, and still later developed osteogenic sarcomas in the irradiated bones, after an average latent period of 25 years. Martland quoted from his earliest article about a girl with exposure to radioactive paint: "Her general physical condition is good and she could at the present time pass a strict medical examination and obtain almost any amount of insurance.... Who can tell when she will develop an acute fatal anemia, or a more chronic anemia with or without crippling bone lesions". Five years later this dial painter had indeed developed an osteogenic sarcoma of the femur with fatal results. The bone marrow, interestingly enough, did not show aplasia but intense regeneration with enormous numbers of erythroblastic and myeoblastic elements suggesting marrow arrest or excessive destruction.

Certain lessons can be learned from Martland's group:

1. The radioactive elements had long half-lives, that of radium being 1650 years and mesothorium 6.9 years.
2. The elements were deposited in bones, a relatively inert tissue so that they were extremely slowly excreted, that is, they had a very long biologic or effective half-life.
3. The elements produced alpha particles, one of the most biologically destructive types of radiation.
4. A considerable latent period existed before eventual development of the malignant changes of osteogenic sarcoma in the damaged bones.

Martland also pointed out the variation in susceptibility, that not all the exposed personnel developed these changes despite receiving equivalent or greater amounts of radiation.

Radiation can produce a serious general effect on the hematologic system. Initially, cumulative exposure to radiation produces a drop in the white cell count, but Stone has cast doubt on

the value of periodic white cell counts in assessing excessive exposure. Aplastic anemia and leukemia have been ascribed to radiation, but these ill effects on the hematologic system described in man have resulted from cumulative exposure as seen in technicians, radiologists or persons concerned with the handling of radioactive materials. While the evidence of the increased frequency of leukemia in radiologists is based on only 14 deaths from leukemia among 299 deaths of radiologists, the increased incidence of leukemia in all physicians and in survivors of the atomic bomb explosions lends significance to the development of leukemia as a general result of radiation.

A recent report describes the development of osteogenic sarcoma in bone that received moderate doses of radiation from 5 to 20 years previously, and also a series of 28 children with carcinoma of the thyroid: of whom 9 had received radiation to the thymus gland.

Another serious consequence of radiation is cataract formation from neutron radiation. Obesity, reduction in life span, impaired fertility and genetic effects possibly may be anticipated, from experimental work on animals. Briefly, the most important late effects to consider in evaluation of a risk who has been exposed to radioactive isotopes is the production of generalized malignant change of leukemia, or local malignant change in the irradiated tissues, and the necessity to keep in mind the long latent period before malignant changes take place.

Despite the inherent risks of radiation, radioactive isotopes are powerful tools to the worker in the fundamental fields of biologic research. By the use of radioactive isotopes it has been possible to trace the distribution, anatomic localization and behavior of the elements in the tissues. By the introduction of a radioactive isotope into compounds to produce a so-called labelled compound, it has been feasible to discover the metabolic pathways of many materials in the body. The majority of this work has been done in an experimental animal and may not be of immediate importance to life insurance medicine. Nevertheless, in the long run, the greatest advantage of radioactive isotopes will be not in their therapeutic usefulness, but in furthering the field of fundamental knowledge.

Inevitably radioactive isotopic tracer technics were extended to the field of clinical investigation in the human. The imagination and ingenuity of the investigators in employing the isotopes have made them useful in nearly all aspects of clinical investigation. As these isotopes are radioactive, certain safeguards in their use have been imposed. The isotope itself must satisfy certain criteria. The mass and number of the isotope, the type of radiation emitted, and the chemical purity must be well known. The half-life cannot be too long because of the radiation hazards, nor too short to make transportation difficult. The element itself cannot be toxic unless a very high specific radioactivity can be obtained. The biologic behavior of the element must be well understood, at least in animals. The most important method of assuring that these radioactive isotopes are not used indiscriminately is one that exists in both Canada and the United States. In each of these countries a committee on isotopes was formed to assist in the distribution of these radioactive elements. The purposes of these committees were to make radioactive isotopes available for use in humans and to protect, as far as possible, the subjects from indiscriminate use of isotopes. To achieve these aims these committees have undertaken to set up certain broad criteria for the allocation of radioactive isotopes. In general, the physician in charge must be associated with a medical institution of good standing and possessing adequate facilities for the care of the patient and the handling of the isotopes. The committee is insistent that the physician must have previous experience with the use of radioactive materials. As well, another safeguard is to require local committees to evaluate all proposals for therapeutic uses of the substances. After satisfying these criteria, the individual must submit an application for approval, showing what isotope he will require and for what use, and what doses he will use on patients to be investigated. These committees are quite conservative in their assessment of the tolerance dose of radiation a patient can receive and are particularly concerned with the use of long lived isotopes.

These entirely necessary restrictions have not prohibited an expansion of the employment of the radioactive isotopes in clinical investigation. Radioactive iodine (I-131) has been extensively employed for over 10 years in the study of normal and abnormal

thyroid physiology in humans and has given us a much clearer concept of the function of the thyroid gland. It has been possible to incorporate radioactive iodine into various proteins, for example serum albumin, so as to produce a tag on the serum albumin. This radioactive iodinated human serum albumin has been used to determine the volume of circulating plasma and the distribution of this protein in the human body. Radioactive iron has been employed to study the absorption of iron in various conditions, and the rate of formation and disintegration of red blood cells. Radioactive phosphorus and radioactive chromium have been employed to tag red blood cells to determine the amount of circulating red cells in the body. Radioactive sodium, radioactive potassium and radioactive bromine have been extensively employed to study the electrolytes in the human body. Radioactive isotope of carbon (C-14) has proved most useful too in the hands of the investigators using animals and plants. Carbon 14 has a half-life of 6000 years, which makes it extremely hazardous to use in human subjects. Fortunately many of the compounds that have been labelled with radioactive carbon are rapidly broken down and the radioactive carbon excreted rapidly, so that in certain selected instances, it has been used in human subjects.

But what about the practical application of these isotopes to the field of human medicine, such as might concern the life insurance companies? In this day a very brief interval separates the field of clinical investigation from the field of practical applicability in laboratory diagnosis. Certain diagnostic procedures that entail the use of radioactive elements are becoming very common today. Perhaps the most widely used of all these tests is radioactive iodine in the diagnosis of thyroid disorders. Radioactive iodine is an almost ideal isotope for use in the human. The half life of radioactive iodine is relatively short, being only 8 days, so that radiation hazard is minimized. After an oral or intravenous dose of radioactive iodine this element is almost entirely concentrated in the thyroid gland or else is excreted in the urine. The amount and rate that radioactive iodine is accumulated in the thyroid gland is in direct relationship to the activity of the gland. In other words, the hyperactive gland of hyperthyroidism takes up more iodine than the normal gland. Conversely, the underacting,

or absent gland, of a person with myxedema takes up little or no radioactive iodine. If the amount in the thyroid gland is estimated 24 hours after giving of the dose, by means of an externally placed counter, it is found that the normal gland contains from 10 to 45 per cent of the ingested dose. In the patient with hyperthyroidism, over 45 per cent of the dose is in the thyroid but in the hypothyroid or myxedematous patient less than 10 per cent of the dose is taken up by the gland. This has provided an excellent test to determine the thyroid function directly. In our hands, and in the hands of many investigators, it has proved to be superior to the conventional basal metabolic rate determination. It is, of course, a laboratory test and as such is not infallible. We have assessed the accuracy as about 90 to 95 per cent which compares very favorably to the accuracy of a much more cumbersome determination, the protein bound iodine of the plasma and much more efficient than the 50-75 per cent accuracy of the basal metabolic rate, as done routinely in most laboratories. Many refinements of technic have been introduced to increase its accuracy, such as the determination of the rate of accumulation of iodine by the thyroid gland, the amount of blood that is cleared of radioactive iodine by the thyroid gland, and the conversion rate which determines the amount of radioactive iodine that is incorporated into the plasma protein bound portion of iodine, that is, the hormonal iodine of the blood. While these tests do deliver an appreciable amount of radiation to the thyroid gland, this is unlikely to be of serious consequence and the amount necessary is being consistently reduced by refinements in technic.

Radioactive phosphorus and radioactive chromium are employed to determine the amount of circulating red blood cells. As well, radioactive iodinated human serum albumin is being increasingly used to determine the circulating plasma volume. Another technic that has been used clinically, is the use of the iodinated serum albumin to investigate persons with suspected brain tumors, as it has been found that this iodinated albumin is concentrated in the area of the tumor. Ordinarily tracer or test doses of radioactive isotopes should not produce any health hazards to the patient who has received them if any reasonable caution is used.

The therapeutic usefulness of these compounds in benign con-

ditions is extremely limited. The most used of these isotopes in benign conditions is radioactive iodine. Radioactive iodine, as you know, is selectively concentrated to a marked degree in the thyroid gland and by virtue of the radiation produced, largely in the form of beta rays, can produce a radiation thyroidectomy. The changes that it can produce in the hyperthyroid gland are characterized by extensive destruction of the follicles and replacement fibrosis. Radioactive iodine has now been extensively employed in the therapy of hyperthyroidism in many centers in North America. Obviously not all the cases so treated have been reported in the literature, but the results in the use of radioactive iodine in the treatment of hyperthyroidism with the conventional surgical treatment of this disorder have been compared. These results are quite comparable. You might ask why we should use a new treatment if we have a perfectly good treatment that has been used for many years. The advantages of radioactive iodine therapy of hyperthyroidism are quite obvious. It does not entail the discomfort and apprehension of a surgical operation. The mortality rate is slightly less and post-operative accidents, such as vocal cord paralysis, are avoided. The necessity for a long period of preparation for the operation, the hospitalization required, and the period of convalescence after the operation, may in many cases be entirely obviated, a point that is of some importance to those who are writing sickness and disability benefit contracts. Unfortunately, as my surgical associates are quick to point out, there are disadvantages to the use of radioactive iodine in the treatment of hyperthyroidism. First and foremost, there is the danger that occurs with any form of radiation, the danger of the production of malignancy. Extensive damage is produced in the thyroid gland, as previously described, by the use of radioactive iodine. The amount of radiation that the thyroid gland receives in the treatment of hyperthyroidism is considerable as compared to certain familiar x-ray procedures. This may serve as the start of malignant changes as we might infer from Martland's cases of malignancy in the dial painters. However, these unfortunate people had ingested a long lived isotope with slow excretion, whereas radioactive iodine has a short half-life and is rapidly excreted so that in no sense are they strictly comparable. Certain experiments with animals, notably the rat, have shown that radioactive iodine

and goitrogens, such as propylthiouracil, together or separately, can produce a condition that is remarkably like metastatic carcinoma. Nevertheless, translating animal experiments into human experience may be fallacious. In the ten years that radioactive iodine has been used for the treatment of hyperthyroidism, there have been no reported cases of malignancy, and for the reasons mentioned, it may not be a very great hazard. Carcinoma of the thyroid did not follow the older method of x-ray treatment of hyperthyroidism. Certain other disadvantages exist, such as the waiting period, extending for 8 weeks or even longer before an appreciable clinical improvement occurs after giving the dose of radioactive iodine. Another disadvantage is the large quantity of radioactive iodine that is required to produce the effects in toxic nodular goitre of large size. Determination of the dose required is uncertain, as it depends on the size of the thyroid which is difficult to estimate properly. In our experience over the past 6 years with radioactive iodine, we have arrived at certain indications and contra-indications to the use of the isotope treatment for hyperthyroidism. Recurrent hyperthyroidism is a definite indication for the use of radioactive iodine because surgical treatment may result in a rather unpleasantly high incidence of surgical complications. Grave's disease, or hyperthyroidism associated with a diffuse toxic goitre in the older age group probably should be treated with radioactive iodine. Patients refusing surgical therapy or who are not suitable for surgical therapy because of associated conditions, or who are some distance from adequate medical attention probably should be treated with radioactive iodine. In short, radioactive iodine appears to be the definitive medical treatment at the present time. Hyperthyroidism occurring in the younger age groups should be treated by surgical means. Patients with large toxic nodular goitres are more satisfactorily treated surgically if they can be adequately prepared for operation. Some workers believe that the incidence of malignancy is sufficiently high in the nodular goitres to warrant surgical treatment, but this danger is likely overrated. While the wholesale use of this agent in the treatment of hyperthyroidism is not advocated, its conservative use is an excellent means of therapy. In the opinion of this writer, persons who have received this treatment could be accepted as standard insurance risks, provided their disease is under control.

One other benign condition for which radioactive isotopes have been used is polycythemia vera. Radioactive phosphorus (P-32) is localized in actively growing cells such as exist in the bone marrow and is also concentrated in the bone, so that the hyperplastic bone marrow is subjected to localized radiation with a reduction in the hyperactivity. Radioactive phosphorus has been used in the treatment of this condition for some time now and appears to be the treatment of choice. Terminal leukemia may be more common in cases treated with P-32 and the fact that leukemia may be a complication of polycythemia vera makes the evaluation of the incidence of leukemia in treated patients extremely difficult. Lawrence has compared his series of cases of polycythemia vera treated by radioactive phosphorus to patients with diabetes and pernicious anemia. Lawrence's cases had an average age at onset of 50.7 years and an average age at death of 64.5 years. In pernicious anemia, the average age at onset was 57 years and average age at death was 67.1 years, and in diabetes, 50.4 years at onset and average age at death of 64.5 years. Thus it would appear that the treatment of polycythemia vera with radioactive phosphorus does not introduce any particular extra hazard.

At first, radioactive isotopes appeared to promise further control of neoplastic diseases. Unfortunately they have not fulfilled this promise except in very rare instances. Radioactive iodine has proved to be one of the most useful of the internally administered isotopes because certain cases of metastatic thyroid carcinoma retain or develop the ability to selectively concentrate enough radioactive iodine to make therapy feasible. Interestingly enough, the use of radioactive iodine in the study of these neoplasms has enabled workers to develop better technics to increase the iodine-accumulating ability of the metastases and enhance the usefulness of this isotope. In our hands it has been of definite, though limited usefulness.

In our series:

14 cases were judged worthy of treatment with the following results:

2 complete resolution

2 resolution but residual masses

4 palliation was obtained, but 2 are dead
2 failure
4 currently being treated

In rare instances certain extremely satisfactory results may be retained. While these results are exceedingly gratifying, it is impossible to claim a cure because of the natural history of the disease. For example, in one case that we treated, the patient was known to have had metastases to regional lymph nodes for some 28 years before treatment with radioactive iodine.

Other isotopes have some value in the palliation of malignant lesions. Radioactive phosphorus has been employed in the treatment of leukemia, especially chronic myelogenous leukemia, but it appears that chemotherapeutic agents will supplant it eventually. Radioactive gold, in a colloidal suspension, has a definite role in the palliation of malignant effusions in peritoneal and pleural cavities. Further developments may extend the use of radioactive isotopes in the treatment of cancer but they are hardly likely to prove the answer to neoplasms.

In summary, it may be stated that radioactive isotopes represent one of the major advances in medicine in the last decade, particularly in basic research. The hazards of radiation have been reviewed and although no convincing evidence of serious after effects are apparent to date, the long latent period may exist before late malignant changes appear. The radioactive isotopes have limited but important roles in the diagnosis and treatment of disease and their use will continue to expand.

PRESIDENT MONTGOMERY — Thank you very much, Dr. Gemmell. I am sure someone will want to ask Dr. Gemmell a question or two.

DR. J. GILBERT FALCONER — Dr. Gemmell, what about the matter of the time of recurrence after the treatment of hyperthryoidism? Is there any general extent of time after which a recurrence is not likely to take place?

PRESIDENT MONTGOMERY — Are there any further questions?

DR. RALPH M. FILSON — Mr. President, it certainly is always a stimulating experience to be exposed to pure knowledge by one

who has contributed to its increase. That, I think, has been our good fortune this morning.

Yesterday from Dr. Farquharson we heard something about the influences of fear and of faith. Possibly some of us in the field of life insurance medicine may be actuated too much by the former and too little by the latter as we contemplate our long range responsibilities in regard to those who have been given incautiously measured doses of radioactive substances. Questions do arise from discussions such as we have just listened to and I have some that I would like to present to Dr. Gemmell. If the answering of these questions involves some degree of repetition of what he has already told us I think probably the emphasis that goes with repetition may be justified on this occasion, because of the really vital importance that this subject has for all of us.

Doctor, can we have confidence that with current knowledge these substances will localize and exert their effects only where desired and needed?

Can we soundly prognosticate that after a specified interval no late or important adverse effects will appear in those exposed?

With given conditions, when their symptoms have cleared as a result of the use of radioactive isotopes, how long a period of absence of symptoms or findings will represent an acceptable measure of the expectation of cure?

Dr. J. Keith Gordon — Would you regard the fairly recent history of treatment with radioactive iodine in the same light as the recent history — we will say two years or three years — of thyroidectomy, for life insurance purposes?

Dr. Gemmell — I would like to reply to Dr. Falconer's question about recurrence.

Now, from personal experience about recurrence from radioactive iodine therapy, I might say that I have not seen what I might call late recurrence. I have seen people that with one dose or even two doses have not been completely cured — certainly not to the extent of surgical thyroidectomy. I have not seen a late recurrence, however.

Because of using radioactive iodine I have had a great deal of experience with recurrent thyrotoxicosis following surgical treat-

ment. This can occur anywhere from a real recurrence in a matter of six months, when they have felt perfectly well for maybe three months, and suddenly it all comes back — or it may extend ten years afterwards.

I think as far as recurrent hyperthyroidism is concerned, it is the patient's fault, not the surgeon's fault. The good thing about radioactive iodine is that you can usually keep up treatment until you get the result you want.

Now, Dr. Filson's questions, which go to the heart of the matter — the first is, can we guarantee that the effects of radioactive iodine are going to be local, or can we have general effects, such as leukemia? Can we have genetic effects? Can we have sterilization occurring?

From my experience, I feel that if we are going to have any ill effects from radioactive iodine, they are going to be local effects. They are going to be effects on the thyroid gland. The amount of radiation that the body receives generally with radioactive iodine is quite reasonable, and I personally have had no fears. I have given much greater doses than this to a woman with pulmonary metastases, a young woman, and when I was just ready to give her the final dose to clear her lungs, she got pregnant, and we thought it best not to interrupt her pregnancy. The fetus was a normal fetus. There was no evidence of any abnormality in the child.

Well, you say, can I guarantee that there are going to be no late adverse effects, and the answer to that is no, I cannot. I cannot guarantee that there will be no late ill effects in any medication we use. No one can. We do calculated risks.

The prize example that I can bring to your mind is the buckets of chloromycetin that were used before we recognized that it was causing aplastic anemia. However, we still use it in a calculated risk fashion and while we cannot guarantee absence of ill effects for the reasons that I have mentioned, I think it is a reasonably good calculated risk to use it.

Now, it has been my policy not to use it on young people for two reasons. One is that young people have much longer to live, and if this has a latent effect, they are going to have a much

longer latent period than older people. I will not define, in deference to some of the physicians here, what I mean by "older age group."

The point is that the older people are not going to be subjected to these carcinogenic agents for a sufficient length of time. They may die of vascular accidents before they develop any malignant changes.

The question is also asked, at what period after giving radioactive iodine can you be reasonably certain that they are cured?

Now, I think that if a person after three months — because I think it takes at least three months to get an adequate effect — and if after three months to twelve weeks they have gained weight and they no longer have tachycardia and their metabolic rate is normal — or whatever test you are using — then I think it is safe to say that they are cured. There may be a recurrence, but probably there will not be.

As for the answer to Dr. Gordon's question, I think a period of three months, or if you want to be conservative, six months, should be allowed to elapse before you write off these cases. I believe this is just about the time that relapse may occur after surgical treatment. Incidentally, I think the number of late recurrences will be minimal. I think you may find for myxedematous people, if they are adequately treated, that is not too great a problem.

Dr. Donald E. Yochem — First I would like to congratulate Dr. Gemmell for his masterful presentation of this complex subject.

There are a few interesting points that I would like to make. I see that the cure rate given on his chart is 75 to 80 per cent in both thyroidectomy and radioactive iodine therapy. I did a statistical study, and arrived at a figure of 85 per cent cure rate in surgically treated cases, and 85 per cent in radioactive iodine treated cases. Therefore, those figures appear valid.

Secondly, the incidence of myxedema was 5 per cent in surgically treated cases, and one to 5 per cent in radioactive iodine treated cases.

Now, it was surprising to me that the death rate was given at 0.1 per cent in radioactive iodine treatment. The Cleveland Clinic and various other large clinics made a study of the death rate and adverse effects of radioactive iodine, and it was reported that there was not one case of death resulting from the use of the radioactive iodine treatment.

Secondly, any carcinogenic effects that might occur would occur in the thyroid. However, after twelve years have elapsed since the first case was attempted, there are still no cases of carcinoma of the thyroid reported following this treatment. Pathological studies did not show any carcinogenic effects.

There was one case reported where there was a slight hemapoetic depression of the bone marrow after massive doses of radioactive iodine treatment.

Now, with reference to radioactive iodine treatment, it is rapidly replacing surgical treatment of hyperplastic or diffuse hyperthyroidism. It is not replacing surgical treatment in nodular hyperthyroidism, where surgery is the treatment of choice.

The next point of interest on radioactive iodine is that $I^{131}$ has almost a specific effect on the well differentiated papillary type of adenoma, but has no effect in the undifferentiated or nonpapillary type of carcinoma. Those cases, once they have become malignant and spread beyond the capsule, can not be treated with radioactive iodine, whether they have spread beyond the capsule or not.

Now, I believe for all practical purposes that we in the life insurance industry can insure persons treated for hyperthyroidism with radioactive iodine from the same standpoint as those treated surgically.

PRESIDENT MONTGOMERY — Thank you, Dr. Gemmell. This has been a most interesting paper, but I believe we will have to move on and terminate this matter. Thank you very much, Dr. Gemmell.

Our second speaker this morning is Dr. Robert M. Janes, Professor of Surgery at the University of Toronto. Dr. Janes was born in Ontario in 1894, and is of Irish ancestry. He graduated from the University of Toronto in 1916 and after spending some

time in the Canadian Army Medical Corps, he returned to the staff of the Toronto General Hospital as Junior Surgeon in 1922, becoming Professor of Surgery of the University of Toronto in 1946.

Dr. Janes is a very good example of his own precept — that all surgeons should be well trained general surgeons before they become specialists, which in Dr. Janes' case is chest surgery. Dr. Janes was one of the pioneers in chest surgery and twenty years ago developed a tourniquet for handling the lung pedicle. This has since been superseded by dissection of each component part. We are very happy indeed to have Dr. Janes talk to us today on the subject of "Insurability After Chest Surgery."

# *INSURABILITY AFTER CHEST SURGERY*

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It is not so long ago that patients and doctors regarded any operation upon the chest, beyond the drainage of an empyema, as a hazardous procedure likely to be followed by at least some disability. If carried out by a proper team possessing adequate facilities, thoracotomy *per se* should involve little if any more risk than laparotomy. The discomfort and pain in the early post-operative period is perhaps somewhat greater on the average than that following operations on the abdomen. Pain from the wound itself may persist for several weeks, but except in rare instances is unlikely to be a cause of disability beyond a period of 6 to 8 weeks providing the psychological management of the patient, as well as the surgery, is properly carried out. It is a great mistake to lead these patients to believe that their discomfort is going to be more than temporary, and equally unwise to suggest that they could expect to have no discomfort, or that it is unusual that they have some pain.

Before discussing the results to be expected from the operative treatment of specific conditions, let us consider the factors that may lead to disability following any thoracic operation. That persisting pain may in a few instances be the cause of prolonged or even permanent disability, particularly in a patient with an introspective temperament, must be admitted. Limitation of chest wall and diaphragmatic movements will lead of necessity to some lessening of pulmonary reserve. Post-operative complications, such as haemothorax and empyema, increase the morbidity and disability. Postural deformity, either kyphosis or scoliosis, interferes with function. Properly controlled chest exercises are, therefore, of great importance. Since post-operative complications were so much more common a few years ago and postural deformities less well controlled, a good many of the patients operated upon in that era

have more disability than the amount of pulmonary tissue lost warranted.

The effect of removal of lung tissue depends upon the conditions of the area removed, the amount removed, and the state of the remainder. Removal of a functionless lobe or lung causes no further loss of function, but thoracoplasty over a functionless lung causes a further reduction[1]. The patient whose ventilatory capacity is already reduced by widespread fibrosis or emphysema is likely to suffer more than the usual disability from removal of a considerable portion of his lung tissue. On the other hand, a patient with emphysema may suffer much less disability from removal of one lung than would have been anticipated, and indeed it has been suggested that the over-distension of the remaining lung which follows if no thoracoplasty is done, may actually increase its functional efficiency. There has been and there remains a difference of opinion among thoracic surgeons regarding whether thoracoplasty should be done as a routine procedure following total pneumonectomy in order to prevent over-distension of the remaining lung.

It has been our belief that over-distension and emphysema should not be confused and that emphysema did not develop as a result of over-distension but was, when it occurred, the progression of a pre-existing disease. Gaesler and Streider[1] found no real evidence that chronic over-distension leads to true pulmonary emphysema and the histological changes characterized by disruption of the pulmonary parenchymal architecture. In the absence of pre-existing true emphysema none developed. The same authors found that thoracoplasty three months after pneumonectomy prevented over-distension but caused a definite additional loss of maximal ventilation. The animal experiments of Longacre and Johansmann[2] suggested that with the passage of years, emphysematous changes might be anticipated in the remaining over-distended lung when the proportion of lung tissue removed had been large. This problem cannot be considered as settled but from a clinical standpoint, the condition of patients who had extensive resections as long as 20 years ago, does not lead one to believe that such progressive changes are occurring. Peters, Ross, Black and Burford[3] carried out respiratory function studies upon 10 children operated upon

from 8 months to 13 years previously, and found no apparent correlation between age at operation and physiological performance, and except perhaps for the first year, the interval after operation did not seem to influence the result. That the best performance on all tests was found in the two most active patients suggested the importance of physical training after pneumonectomy and the maintenance of a mobile diaphragm and mediastinum.

Cournand, Riley, Himmelstein and Austrian[4] demonstrated that a state of mild pulmonary hypertension inevitably develops in the course of mild exercise when the entire right ventricular output circulating through a single lung reaches an easily obtainable level, and that in the course of strenuous exercise, the blood flow through a single lung may reach high values and may result in a state of very marked pulmonary hypertension. However, in patients studied, the mass of the right ventricle had not increased and, therefore, right ventricular hypertrophy had not developed after several years, although the subjects had not restricted their physical activity.

Patients who had the older type of thoracoplasty performed for empyema some years ago, operations of the Schedé and Estlander type, suffered a very great and perhaps complete disability because of paradoxical movements of an unstable chest wall. Thoracoplasty for chronic empyema rarely becomes necessary today and the more modern operations leave a stable chest wall. Large defects do result, however, from extensive removal of big chest wall tumors. It is amazing how little disability some such patients have but those who do suffer respiratory embarrassment from paradoxical movement should be relieved by a suitable stabilizing operation.

*Bronchiectasis*

It is accepted that bronchiectasis is a disease in which irreparable damage has been done to the involved portions of the bronchial tree, that spontaneous cure cannot be anticipated, and that all forms of treatment other than surgical are palliative. In some patients the condition is undoubtedly progressive; more often the areas involved become more severely damaged and in a small number of cases, there is undoubtedly an extension to previously healthy portions of the tree. Most figures as to prognosis without surgical treatment apply to the pre-antibiotic era when various follow-ups

showed a morality as high as 40 per cent in untreated cases in a 5 year period. Undoubtedly the control of acute exacerbations of the infections with antibiotics has improved the prognosis without operation as well as rendering operation safer.

The indications for operation are relatively simple in that all patients in the younger age groups (say below 40 years) should have the diseased area removed, providing it is not so extensive that its removal is likely to reduce the respiratory capacity to such an extent as to leave the patient a respiratory cripple. The process rarely extends post-operatively to involve previously normal bronchi unless the operation is complicated by obstruction of a bronchus to a remaining segment of lung. It is vitally important that all portions of the bronchial tree be visualized in the bronchogram before operation is undertaken. In the absence of post-operative complications, most so-called extensions of the disease represent a previously unrecognized area, and re-study of the bronchograms in the light of the new ones showing disease convinces one that the films were misinterpreted or that the apparently new area had not filled in the original film. A small amount of residual disease does not always produce symptoms and the management of a patient with extensive disease on one side and minimal upon the other requires some judgment. Rosemond, Burnett and Long[5] in 1951 reviewed the results of operation on 159 patients operated upon between 1936 and 1949 and followed for 1 to 15 years. One hundred and eighteen were free of cough; of these 14 had residual disease. Of 55 patients with residual disease, 14 or 25.5 per cent had no cough or symptoms, 36 or 65.5 per cent had less cough; and 5 or 9 per cent had increasing cough. That untreated disease is still hazardous was shown in discussion by Scanlon[5] when he reported 19 patients seen between 1939 and 1940 with disease anatomically suitable for excision but not operated upon. Eleven were in excellent health but 4 had died of fatal pulmonary haemorrhage and one of general decay.

In 1950 Kergin[7] analyzed the results of surgical treatment in 58 bilateral cases, 31 of which had had bilateral excisions. There had been 4 deaths in the first 13 cases but no operative mortality in the last 18 consecutive cases. Two of these deaths were from sepsis (1 empyema and 1 brain abscess) in the pre-antibiotic days,

and 2 from cerebral anoxia when the importance of maintaining proper oxygenation was poorly understood by the anaesthetist. Of the 27 surviving cases, 1 was unemployable because of respiratory disability. None of the remainder complained of shortness of breath, but most admitted it on questioning. One who had had excision of both lower lobes, the middle lobe and the lingula, was doing heavy work as a steelworker, one was a crane operator, the others were doing light work. One operated upon in 3 stages, each followed by empyema between 1934 and 1936, had worked continuously as an office worker and was not conscious of disability. The removal of one whole lung in the presence of a normal contralateral organ produces little disability.

From the insurance standpoint, therefore, it would appear that patients who have had the disease (bronchiectasis) removed completely are probably as good insurance risks as other members of the community of a similar age group, providing the operation has not been so extensive as to result in serious respiratory disability. Those who have residual disease probably fall into the same category as those who have not been operated upon providing the excision has not been too extensive and removal of the remaining disease is anatomically possible. Very extensive excisions of lung have not been done sufficiently long to give a complete prognosis so far as degenerative disease in the remaining pulmonary tissue and the effects of pulmonary hypertension are concerned, but there seems to have been little progression of disability in a period of 20 years following operation. One of my patients who had a single lobectomy in 1947 at the age of 66 years is still alive and well without disability. It would appear that the prognosis following complete removal of disease even in patients of advanced years, is good providing they are otherwise well.

*Tuberculosis*

Of all the operations that have been advocated for the treatment of pulmonary tuberculosis, only two are used widely today, thoracoplasty and some form of resection. Thoracoplasty has been effective over many years and will always have a place, but recently, with new and better technics and more effective antibiotics, excision is gaining in favor. Thoracoplasty has the dis-

advantage of being in most instances a staged operation and productive of much discomfort, but it is also ineffective in the management if solid lesions (the so-called tuberculomas), tuberculous bronchitis, bronchostenosis, atelectasis, and large non-collapsible cavities. In addition, it inevitably sacrifices much healthy tissue, often for the control of a relatively small area of disease. On the other hand, it is a safe method of therapy and with a careful selection of cases has given excellent results. Between 1943 and 1952 at the Toronto Hospital for Tuberculosis, 1144 thoracoplasty stages were done on 615 patients with 7 post-operative deaths, a stage mortality rate of 0.61 per cent and a case mortality rate of 1.14 per cent. Its effectiveness when combined with recent medical therapy is illustrated by the fact that at the same institution only 2 of 82 patients treated by thoracoplasty in 1951 have continued to have positive sputum on culture. Over many years before excisional therapy was widely used and when many far from ideal cases were accepted for operation, 85 per cent sputum conversion was obtained. Long term follow-ups on patients treated by thoracoplasty even in the pre-antibiotic days showed that few arrested cases were re-activated. In 1953 Aufses and Hart[8] reported upon 90 cases previously reported in 1941. Only 4 of 64 cases considered inactive in 1941 had shown reactivation in this 12 year period and one of these had again been arrested. Long term results in patients that have had the advantage of antibiotic therapy may be expected to be much better. When resection is undertaken, it may be pneumonectomy, lobectomy, lobectomy plus a segmental resection, segmental resection alone, or a simple wedge removal of a local area. Frequent application of segmental and wedge resection has been made possible in the last few years by the antibiotics, especially when they are used in combination. Whether these have become so effective that resection of small nodules and tuberculomas as presently practised is unnecessary remains to be seen. Many of the latter when discovered accidentally will continue to require exploration because of the impossibility of certain diagnosis but when they are known to be the end stage of pre-existing disease, this reason does not exist. The operative mortality at the Toronto Hospital for Tuberculosis from the various types of excision therapy in the pre-antibiotic era was 18.6 per cent. Recent mortality in 24 cases

with streptomycin resistant organism was 8.3 per cent but in 133 cases negative for tubercle bacilli (or with streptomycin sensitive organisms) there was no mortality. This type of treatment may be said, therefore, to be relatively safe but whether the excision of local lesions to prevent recrudescence of the disease will continue to be necessary, only long term experience of the effectiveness of drug therapy will determine. Of 200 patients treated by pulmonary resection at the Toronto Hospital for Tuberculosis prior to January 1953 and followed from 1 to 12 years, 6.5 per cent had had a recurrence of the disease but had recovered, and only 2.5 per cent were suffering from active tuberculosis at the time of the report. Ten had died from tuberculosis, 6 within the first year after operation and 4 from 1 to 6 years after operation from progression of the disease in the opposite lung. It is to be expected, therefore, that the long term results in those that have had the protection of antibiotics will be very good.

*Bronchogenic Carcinoma*

Carcinoma of the lung leads all other causes of death from pulmonary disease in white males.[9] In the province of Ontario during 1952 there were 578 registered deaths from primary carcinoma of the lung as compared to 371 deaths directly attributable to tuberculosis. One suspects that this includes a certain number of cases of broncheolar or alveolar-celled carcinoma of the lung but this condition presents a similar problem. It may also include some secondary carcinomas but even allowing for all possible errors, the increase in the incidence and mortality of this disease is appalling.

Unfortunately there has not been a corresponding change in the results of treatment. Anaesthesia and surgical technic have improved and there has been some decrease in operative morbidity and mortality. Extension of the operative procedure to accomplish a more radical resection of the area of lymph drainage does not seem to have affected the results appreciably. The operative mortality when resection has been accomplished is at present around 16 per cent in our clinic. Approximately 30 per cent of those that survive resection live three years and about 23 per cent five years. These figures would, at first sight, give some encouragement but when one remembers that only 1 in 3

patients seen in hospital will be considered operable and only 2 of every 3 of these will have resectable lesions, one finds that 1 in 5 of all individuals will have their tumor removed. Of these, about 1 in 4 will be alive at the end of 5 years. While there is some evidence that radiotherapy has had a delaying action upon the course of the disease, results of such treatment do not compare with those obtained by surgery. It is possible that some further improvement in survival statistics may follow a combination of the two methods.

There is not enough evidence available as yet to assess the result that may be expected from excision of broncheolar carcinoma but Storey[10] believes that it may be better than in other forms of lung cancer.

The results of excision of adenoma of the bronchus may be expected to be good. All patients with purely local disease should be cured and the outlook is surprisingly good even in the presence of some lymph node invasion. Complications of the disease are, however, severe and almost certainly at least some growths undergo malignant change. All patients should, therefore, be operated upon: there is no place for bronchoscopic removal.

*Lung Abscess*

Antibiotic therapy has reduced the incidence and mortality of lung abscess. Increasing long term experience has made one somewhat less optimistic of the so-called cures obtained by symptomatic treatment and drainage. It has been learned that fibrous and epithelial lined cavities in lung tissue may not be visible in the x-ray when there is no surrounding zone of inflammation. As years have gone by, an increasing number of these patients have had flare-ups which necessitated resection of the lesion. The tendency today is to treat all patients with lung abscess with massive doses of appropriate antibiotics and to provide external drainage as a life saving measure only when bronchial drainage is ineffective and toxicity is not controlled by the drugs. Those that pass into a stage of chronicity are treated by segmental resection or lobectomy; rarely by pneumonectomy. Recurrence of disease should be rare in the future and disability should persist only in those patients who had pre-existing pulmonary disease or where the volume of lung tissue sacrificed is of itself important.

It would be impossible in any reasonable time to review the results to be expected from the surgical treatment of the many less common conditions. All the diseases that affect bone elsewhere also affect the ribs. The incidence of malignancy and the tendency to malignant change, particularly in benign cartilage growths, is rather high. Perhaps because anatomy permits of a wide removal, the results of adequate surgical excision are good. Tumors and cysts of the mediastinum are relatively uncommon but interesting because of their great variety and because so many of them are or may become malignant. They should be removed when found, the mortality should be negligible, and there should be no disability. Prognosis depends, of course, upon the pathology of the lesion but when complete removal has been possible, results have been surprisingly good, even in some malignant varieties. The commonest benign tumor of lung is the hamartoma. It requires removal because it cannot be differentiated with certainty from malignant conditions. They are known to increase in size and they may obstruct the bronchi. With one possible exception no instance of malignant degeneration has been recorded. Local resection is all that is necessary. Arteriovenous fistulae in the lung are uncommon but interesting and of some importance because of the increasing disability which they produce and the liability of the patients to cerebral complications and bleeding. It is important to remember that they may be multiple and the experience of Charbon, Adams and Carson when they found themselves called upon to treat a lesion in the remaining lung of a patient who had had the left lung removed 6 years before, indicates that no more extensive removal should be done than is necessary to deal with a particular lesion. There is often more than one and each may be treated by local resection. In those very extensive lesions involving a whole lobe or lung, massive resection of lung is, of course, a necessity. Complete removal results in cure, and unless the amount of lung sacrificed is of itself important, no disability.

One may only mention the surgery of trauma but it is important to remember that although the indication for major surgical interference in such cases is infrequent, early and adequate operative treatment may, when indicated, not only save life but prevent permanent disability. Spontaneous pneumothorax should not be

allowed to recur indefinitely because it endangers life, produces disability and in many instances, can be cured by surgery.

*Oesophagus*

Great technical advances have been made in surgery of the oesophagus in the past fifteen years. As Mustard says, "Oesophagectomy with replacement has advanced from being a surgical adventure rarely successful to its present status as a well established technic with a preponderance of successful results".[13] In many conditions the results of treatment have been as gratifying as the technical advance but unfortunately this is not universally true.

In the field of trauma, accidental perforation of the oesophagus by an instrument is much less lethal and many cases have recovered with the use of an indwelling tube and antibiotics. An increasing number of recoveries from spontaneous perforation of the oesophagus are being reported: there was no recorded instance of recovery before 1946.[6] From an insurance point of view, it is worth noting that this peculiar accident happens in a previously normal organ and cases diagnosed early and successfully operated upon are likely to be quite well. Strictures that fail to respond to dilation may be resected but results are dependent upon the factors to be described later.

The majority of benign tumors may be enucleated with successful results. Diverticula, whether of the pharyngo-oesophageal or intrathoracic variety, may be operated upon successfully with a minimum of danger and with every expectation of cure.

Cardiospasm or achylasia of the oesophagus is still imperfectly understood. The majority of cases may be managed by dilation alone. Olsen[14] and associates reported the Mayo Clinic experiences from January 1935 to January 1947. In about 80 per cent of cases, permanent relief was obtained from dilatation with the hydrostatic bag. Many of the remaining 20 per cent were improved but still had some dysphagia, some required repeated dilatations. A very small number of the group were treated surgically. In general, it may be said that any operation which destroys the cardiac sphincter thus allowing regurgitation of gastric contents into the oesophagus, is followed frequently by oesophagitis and

the results are unsatisfactory. The most popular operation at the moment is a modification of the procedure described by Heller many years ago which consists in a division over a wide area of the muscle of the oesophagus and adjacent area of the cardia down to the mucosa — much like the Ramnstedt operation for pyloric stenosis. No patient who can be managed by dilation should be operated upon.

Great progress has been made in the understanding and treatment of diaphragmatic hernia. Failures in the development of the diaphragm account for the majority of herniae in childhood. Seventy-four per cent of untreated cases die in the first few weeks of life. Mortality from operative repair in early infancy is high but successful repair restores the infant to normal. There seems to be a considerable difference of opinion regarding the success of operations for hiatus hernia in children. Repair of the para-oesophageal type is pretty universally successful. Gertz, Regout and Thomsen[15] reported the results of operation on 60 cases. The para-oesophageal type were cured but not less than 50 per cent of the sliding type showed some radiological evidence of recurrence and only 25 per cent of the patients could be regarded as completely cured. The technic which they describe is probably responsible. Allison[16] has made most important contributions of our knowledge of this condition in recent years. He has emphasized what is pretty generally accepted among surgeons interested in this field today, that the short oesophagus is usually a complication of the sliding hernia, the latter being the primary condition. It is probably true that all cases of sliding hernia that are associated with symptoms, particularly with symptoms of oesophagitis, should be operated upon before stricture of the oesophagus develops as a result of the chronic irritation, and before peptic ulcers occur in the herniated portion of stomach. The truth of this statement remains to be proved by further long term experience of those doing an efficient repair. Undoubtedly the outlook in many untreated cases is increasing disability from distress and bleeding from peptic ulceration and from stenosis of the oesophagus.

In concluding, one should emphasize that the field of thoracic surgery is relatively new and that while efficient technics for

dealing with many of its problems have been perfected in the past few years, much is yet to be learned. It will be necessary for groups such as this to remain familiar with improvements as they occur if they are to assess fairly applications for insurance coverage from individuals who have had chest surgery. Specific reference to many conditions has not been possible in this brief summary but at least the more common problems have been mentioned.

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PRESIDENT MONTGOMERY — Thank you very much, Dr. Janes. I am sure someone will have some questions to ask.

DR. NORMAN J. BARKER — I would like to ask Dr. Janes if it is usual or common to find bronchiectasis so confined — so entirely confined — to one lobe that after lobectomy it can be assumed that the rest of the lung is relatively or completely free of disease?

I would also like to ask him whether the mechanical effects of total pneumonectomy on the cardio-respiratory apparatus, entirely apart from the disease necessitating the operation, has any effect upon the individual's life expectancy.

DR. MONTGOMERY — Any other questions? I think we might as well get all the questions.

QUESTION — Mr. Chairman, I would like to ask Dr. Janes about lung abscess. Is there any reason for our current practice at the present day of putting in a small rider for the first year or so after apparent complete recovery? Apparently some of them do recur, and some of them are not completely cured, and I should like to have his opinion as to whether a very small rider would cover that, or whether it is necessary.

PRESIDENT MONTGOMERY — Any other questions?

DR. KARL ANDERSON — Dr. Janes, have you any figures about the percentage of tumors of the lung that are malignant? You spoke about the number of benign tumors of the lung. Do you have any figures on the total number of tumors in the lung, and what percentage of them turn out to be malignant?

PRESIDENT MONTGOMERY — Any other questions?

DR. JANES — I have no figures as to the exact number of cases of bronchiectasis that are localized to one lobe, but I should say that something like 50 per cent of them are localized nearly or completely to one lobe, and of course there is a considerably higher percentage that are localized to one lobe, or to a lobe and a portion of the adjacent lobe.

For instance, about 65 per cent of lower lobe disease is also associated with involvement of the lingula of the upper lobe on the left side. So that it is really a very high percentage of them, and I have a feeling that as time goes on that percentage will be somewhat higher, because we are not seeing so many of the old, very extensive cases.

Regarding the life expectancy, I do not believe we can answer that fully yet. Our earliest extensive resections were done only 20 years ago, and those patients still seem to be well, and not be developing secondary changes in the remaining lung.

We know that there has been much discussion upon the necessity of doing thoracoplasty on patients that had pneumonectomy for whatever reason, and many clinics have done thoracoplasty almost routinely, at least, to protect the remaining lung. Well,

we have not done that. We now have a large series of patients who have had excision of one lung for one reason or another. Unfortunately the number of cancer cases is not too big, but we do not believe that the overexpansion of the lung in itself produces late changes.

As to the effect of pulmonary hypertension, I think that will have to remain for further experience. The analysis of cases today does not suggest that it will be an important factor in life expectancy.

As to the prognosis from lung abscess, I am afraid that up until now, at any rate, it has been justifiable to put on a small rider, because there is not any doubt about the fact that in quite a lot of the lung abscesses which I saw get better spontaneously years ago, and unfortunately quite a number that I cured through drainage through the chest wall, have come back in later years and have had to have lobectomy done. That in itself is not very dangerous. The risks of bleeding from drained abscesses, which used to be so great in these patients, now seem to have become relatively small with the use of antibiotics.

As to the proportion of malignant to benign tumors, of course an overwhelming proportion are malignant, and one would have to say something about the picture presented. In the case of a single, isolated lesion in the lung in the patient, middle-aged and beyond, I suppose that today something like 50 per cent of them would be malignant. That is a guess. It depends upon the incidence of tuberculosis.

Quite a large percentage of the single lesions turn out to be tuberculosis. Some of them turn out to be teratomas, but that is a very rare disease. Certainly the percentage is high enough so that unless it is known that the disease is not malignant, they must all be explored.

In our series, I think that perhaps there would be one adenoma of the bronchus to 20 or 25 carcinomas.

PRESIDENT MONTGOMERY — Thank you very much, Dr. Janes.

Our next speaker is Dr. Hans Selye, Professor and Director of the Institute of Experimental Medicine and Surgery at the University of Montreal. Dr. Selye was born in Austria in 1907.

He comes from a medical family, as his father was a noted doctor and his grandfather and great grandfather were also physicians. His education was gathered from many sources, the Charles University of Prague, the Universities of Paris and Rome and Johns Hopkins University. In 1932 he went to the Department of Biochemistry, McGill University, Montreal, as a Rockefeller Research fellow where he first developed his evidence for his stress theory of disease in 1936. In 1942 he was awarded his Doctor of Science in Medical Research. He left McGill in 1945 to take his present post at the University of Montreal. After more than 15 years of research, Dr. Selye has demonstrated that diseases of the heart and kidneys, arthritis, and circulatory disturbances have a common denominator which he recognizes as stress, leading to over-adaption and over-production of adrenal hormones.

Dr. Selye has published nearly 400 scientific papers and is the author of a textbook on endocrinology. We are indeed honored today to have Dr. Selye speak to us.

# RECENT ADVANCES IN THE STUDY OF STRESS*

HANS SELYE, M.D., Ph.D., D.Sc., F.R.S.C.
*Professor and Director of the Institute of Experimental Medicine and Surgery*
*University of Montreal*

It is indeed a pleasure to have received your invitation to speak to you today about our work on stress. As I was listening to the very clear-cut, extremely practical and useful presentation of Dr. Janes, I was somewhat worried that, by contrast, my report concerning experimental work on stress might be too far removed from the immediate interests of this group. Yet, stress is undoubtedly an important factor in insurance medicine, and while I am not competent to analyze our findings in terms of your practical interests, I think it will help to clarify our views on this topic if we discuss them briefly together on the basis of our laboratory experiments.

*Precursors of the stress-concept* — Ever since man used the word "disease" he had some, at least subconscious, inkling of the stress concept. The very fact that a single term can be used to denote a great variety of individual maladies clearly indicates that they have something in common. They possess, as we would now say, some non-specific features which permit one to distinguish disease from the condition of health. Yet, precisely because these manifestations are not characteristic of any one disease, they have received little attention in comparison with the specific ones. They were thought to be of lesser interest for, unlike the latter, they did not help to recognize the "eliciting pathogen" or lend themselves to any effective type of specific therapy.

Nevertheless, several early investigators have attempted to elucidate the mechanisms involved in such non-specific reactions. Since our knowledge of the nervous system antedates, by far, the development of modern endocrinology, it is understandable that,

*This summary is based upon the introductory chapter of the "Fourth Annual Report on Stress — 1954" (Acta, Inc., Medical Publishers, Montreal), and served as a text for the lecture as given in Toronto on October 13, 1954.

among the two great integrating systems of the body, the nervous and the hormonal systems, the former was the first to be examined from this point of view. Ricker, Speransky, Reilly, Hoff and many others have gathered important data concerning the role of the nervous system in such non-specific reactions as fever, polymorphonuclear leucocytosis, inflammation, and others. In the domain of what may be called "physiologic stress," W. Cannon's studies helped us to understand the part played by the sympathetic nervous system and its humoral effector substances.

Furthermore, quite independently, a great deal of progress has been made in the study of pituitary and adreno-cortical hormones by chemists, physiologists and clinicians, too numerous to mention by name.

All the knowledge acquired as a result of these early investigations was indispensable for the eventual formulation of the stress-concept, whose leading motive is one of unification. Additional experiments had to be performed, however, to show that the many non-specific responses of individual target organs are closely integrated and actually represent part of a single biologic response, the general adaptation syndrome. These investigations, which will be outlined below, made it evident that the "stress pattern" of reaction plays an integral part in the most varied physiologic, pathologic and pharmacologic phenomena.

*The concept of stress* — By a series of experiments on animals, it was demonstrated in 1936 that the organism responds in a *stereotypical* manner to a variety of widely different factors, such as: infections, intoxications, trauma, nervous strain, heat, cold, muscular fatigue or x-irradiation. The specific actions of all these agents are quite different. Their only common feature is that they place the body in a state of general (systemic) stress. Hence, we concluded that the stereotypical response, which is superimposed upon all specific effects, represents the somatic manifestations of non-specific "stress" itself.

But what is *non-specific "stress"?* The term had long been used in physics to denote the interaction between a force and the resistance opposed to it. For instance, pressure and tension can put inanimate matter under stress. The above mentioned non-

specific response was thought to represent the biologic equivalent of such physical stress. The term has now been quite generally accepted in this sense not only in English, but — since attempts to translate "stress" led to much confusion — also in most other languages.

*The concept of the G-A-S* — The most outstanding manifestations of this stress-response were: *adreno-cortical enlargement* with histologic signs of hyperactivity, *thymico-lymphatic involution* with certain concomitant changes in the blood-count (eosinopenia, lymphopenia, polynucleosis) and *gastro-intestinal ulcers,* often accompanied by other manifestations of *damage or "shock."*

We were struck by the fact that, while during this reaction all the organs of the body show involutional or degenerative changes, the adrenal cortex actually seems to flourish on stress. We suspected this adrenal response to play a useful part in the systemic, non-specific adaptive reaction, which we visualized as a "call to arms" of the body's defense forces and named the "alarm reaction" (Selye, 1936a).

Subsequent studies showed that the alarm reaction is but the first stage of a much more prolonged *General Adaptation Syndrome* (*G-A-S*). The latter comprises three distinct stages, namely:

(1) *the alarm reaction (A-R),* in which adaptation has not yet been acquired.

(2) *the stage of resistance (S-R),* in which adaptation is optimal.

(3) *the stage of exhaustion (S-E),* in which the acquired adaptation is lost again.

*The mechanism of the G-A-S* — In order to elucidate the kinetics of this syndrome we proceeded as follows:

Rats were *adrenalectomized* and then exposed to stressor agents. This showed us that in the absence of the adrenals stress can no longer cause thymico-lymphatic involution or characteristic blood-count changes (Selye, 1936b).

When adrenalectomized rats were treated with the impure *cortical extracts* available at that time, it became evident that thymico-lymphatic involution and the typical blood-count changes could

be produced by adrenal hormones even in the absence of the adrenals. Therefore, these changes were considered to be indirect results of stress mediated by corticoids (Selye, 1936b, 1946).

Conversely, the gastro-intestinal ulcers and other manifestations of pure damage or shock were actually more severe in adrenalectomized than in intact animals and could be lessened by treatment with cortical extracts. It was concluded that these lesions are not mediated through the adrenal; in fact, they are actually combated by an adequate adreno-cortical response to stressor agents (Selye, 1936b).

But what stimulates adreno-cortical function during stress? In the course of the next year, we found that among many surgical interventions tried, only *hypophysectomy* prevents the adrenal response during the alarm reaction. Hence, we concluded that stress stimulates the cortex through an adreno-corticotrophic hormone, now known as ACTH (Selye and Collip, 1936, Selye, 1937).

Then pure cortical steroids became available, thanks first of all to the classical investigations of Kendall and Reichstein. With these, we could show that administration of *mineralo-corticoids* or *M-Cs* (such as desoxycorticosterone) produces experimental replicas of the so-called *hypertensive and inflammatory "rheumatic" diseases*; *notably, nephrosclerosis, hypertension, vascular lesions* (especially periarteritis nodosa and hyalin necrosis of arterioles) (Selye and Pentz, 1943) as well as arthritic changes resembling, in acute experiments, those of rheumatic fever and, after chronic treatment, those of rheumatoid arthritis (Selye et al, 1944). Yet, even very high doses of mineralo-corticoids did not induce any noteworthy thymico-lymphatic or blood-count changes, such as were caused by cortical extracts.

Significantly, exposure of animals to certain non-specific stressor agents (e.g., cold) produced marked adreno-cortical enlargement and organ changes very similar to those elicited by the administration of mineralo-corticoids (Selye, 1943). Still, many investigators doubted that secretion of *M-Cs* could be involved in the pathogenesis of disease, since the very existence of natural, endogenous *M-Cs* was questioned. Indeed until quite recently some of the most eminent students of the adrenal advocated the

"Unitarian Theory", which held that the gland secretes only one corticoid, so that a derangement in the balance between antagonistic cortical hormones would be impossible. This concept was definitely disproven by the isolation of *aldosterone* from both the tissue and the venous blood of the adrenals (Simpson et al, 1953).

Extracts rich in *gluco-corticoids or G-Cs* (such as cortisol and cortisone) on the other hand, were highly potent in causing *thymico-lymphatic* involution and in eliciting the characteristic blood-count changes of the alarm reaction. They also tended to inhibit the inflammatory "rheumatic like" changes which can be elicited in animals by mineralo-corticoids. Thus, in many respects, the two types of corticoid hormones antagonize each other (Selye, 1946, 1950).

Another interesting activity of the corticoids, discovered at about this time, is their singular effect upon the *central nervous system* of animals. A variety of steroids, among which figured both G-Cs (e.g., cortisone) and M-Cs (e.g., DCA), as well as other steroid hormones, and hormone-metabolites (e.g., pregnanediol, pregnanedione), proved to possess the property of causing a state of great excitation and confusion, followed by marked depression of all reflex activities and, eventually, deep anesthesia (Selye, 1942). This observation raised the question whether a pronounced increase in the activity of endogenous corticoids could be responsible for certain nervous and emotional accompaniments of exposure to stress. After the introduction of cortisone into clinical therapy, it became evident that, in man, this hormone can also exert a powerful effect upon the central nervous system. In animals, both G-Cs and M-Cs exhibit this effect, hence we shall have to watch for it as soon as patients will be treated with large doses of aldosterone.

The terms "gluco-corticoids" and "mineralo-corticoids" emphasize the salient metabolic actions of these substances; from a clinical point of view, however, their effects upon inflammation are perhaps of even greater interest. Since the gluco-corticoids inhibit inflammation, while the mineralo-corticoids enhance it, the G-Cs may appropriately be called *"antiphlogistic corticoids"* or *"A-Cs"* and the M-Cs *"prophlogistic corticoids"* or *"P-Cs,"* when they are discussed with reference to their effects upon inflammation. It remains to be seen, however, whether G-C and A-C (or M-C and P-C) activities necessarily run parallel in all steroid compounds, including those (like aldosterone) which have not yet been fully examined for these effects.

*Inflammatory granulomas,* especially those produced in the vicinity of joints by the local application of irritants (e.g., formalin, mustard powder), as well as certain allergic reactions, are likewise

aggravated by P-Cs and inhibited by A-Cs. Apparently, the response of the adrenal cortex is most important not only in defense against systemic stress (affecting the whole organism), but also in the manifold topical defense reactions which occur upon exposure to *local stress* (e.g., bacterial or chemical irritants, response of a "shock organ" to an allergen) (Selye, 1949a, 1950). These findings helped to formulate the concept of the Local Adaptation Syndrome (L-A-S) to be discussed below (cf. p. 12).

In this connection, the hormone sensitivity of certain so-called *"anaphylactoid inflammatory reactions"* is of special interest. Actually, our attention had first been called to a possible relationship between the adrenal cortex and inflammation by an incidental observation on rats, given parenteral injections of egg-white. It was found that the rat is naturally hypersensitive to egg-white, and responds to the intraperitoneal or intravenous administration of this substance by an acute serous inflammation of the paws and snout. This inflammatory response was greatly aggravated in adrenalectomized animals (presumably because they could not defend themselves by the endogenous production of A-Cs). On the other hand, it was prevented by treatment with systemic stressors, directly in proportion to the adreno-cortical enlargement they produced (presumably, as a result of excess A-C secretion) (Selye, 1937). Subsequently, it could be shown that cortisone and ACTH inhibit, while certain crude anterior-pituitary preparations and desoxycorticosterone aggravate this anaphylactoid type of acute inflammation (Selye, 1949b).

Curiously, our crude *anterior pituitary extracts* also duplicated most of the above mentioned actions of P-Cs upon the *cardiovascular system, the blood-pressure, the connective tissue (inflammation), and the kidneys* (Selye, 1944, 1946). The kypophyseal preparations which we used, were definitely corticotrophic, in that they enlarged the adrenal cortex, but they were particularly rich in the so-called "growth hormone" or *somatotrophic hormone (STH).* This made it difficult to interpret our early experiments, in which such crude extracts were used, because we were unable to distinguish clearly between the effects of ACTH and STH. However, as soon as we obtained purified ACTH, it became evident that the above mentioned pathogenic actions of the crude anterior-pituitary preparations could not be due to their ACTH content, since even the highest tolerable doses of the pure corticotrophic hormone failed to duplicate their predominant P-C effects. On the other hand, overdosage with purified STH caused cardiovascular and renal lesions, virtually identical with those previously observed in animals treated with P-Cs. It was then concluded that, probably, the characteristic actions of our crude anterior-pituitary

preparations were mainly due to their STH content. It remains to be seen to what extent STH acts indirectly by stimulating the P-C production of the adrenal cortex, or directly by sensitizing the peripheral tissues to P-Cs. Preliminary observations suggest that the last-mentioned mechanism is more important although both may be implicated (Selye, 1951a). This point is not yet settled.

From the internist's point of view, perhaps the most interesting role of STH in the adaptation syndrome is that it can effectively *combat catabolism and susceptibility to infections.* Animals heavily overdosed with ACTH or A-Cs, tend to lose a great deal of weight. Eventually they die, almost always as a result of generalized septicemia, caused by normally saprophytic micro-organisms. In rats, the lung tissue appears to be singularly predisposed to such infections. Under these conditions, adequate doses of STH prevent the loss of body-weight as well as the excessive microbial proliferation (Selye, 1951b). It remains to be seen to what extent these actions of STH will prove to be of value in the management of infections in man, but experiments on rats have already demonstrated the great influence of adaptive hormones upon resistance to the human type of tuberculosis. Normally the rat is virtually resistant to tuberculosis bacilli; it may be rendered sensitive by ACTH or A-Cs and this sensitivity can, in turn, be abolished by STH (Lemonde et al, 1952a, 1952b).

*Conditioning of hormone actions* — As work along these lines progressed, it became increasingly more obvious that the activity of the hormones produced during stress depends largely upon a variety of "conditioning factors." Both the production of the "adaptive hormones" and their effect upon individual target organs proved to be greatly influenced by heredity, age, previous exposure to stress, the nutritional state, and other factors. Thus, for instance, the production of corticotrophic hormone by the pituitary is enhanced by a high-protein diet, while the action of M-Cs upon most target organs is augmented by excess sodium (Selye, 1946).

Stress itself is perhaps the most effective and most common factor capable of conditioning the actions of adaptive hormones. Thus systemic stress augments the antiphlogistic, lympholitic, catabolic and hyperglycemic actions of A-Cs, while the salient effect of the adaptive hormones, that of modifying the course of inflam-

mation, naturally cannot manifest itself unless some topical stressor first elicited a phlogistic response.

Ingle (1951) introduced the concept of the "permissive actions" of corticoids. This term implies that the adrenal hormone does not affect a target of stress itself, although it permits a stressor to act upon it. Furthermore, allegedly the presence or absence of a permissive factor can only allow or disallow a reaction, but is unable to vary its intensity. To illustrate this concept, one might compare the production of light by an electric lamp to the biologic reaction and the switch to the "permissive factor." The switch cannot produce light, nor regulate the degree of its intensity, but unless it is turned on, the lamp will not function. Correspondingly, the functional signs — generally considered to be characteristic of corticoid-overproduction during stress — would not result from any actual increase in corticoid-secretion, but from the extra-adrenal actions of the stressors themselves. The presence of corticoids would be necessary only in a "supporting capacity" to maintain the vitality and reactivity of tissues.

Actually, it is precisely in the specific and not in the non-specific stress-reactions that the corticoids play a purely "permissive rôle" of this type. Here they are necessary only to prevent stress and collapse thus keeping the tissues responsive. For instance adrenal-ectomized rats will not respond to injected STH with somatic growth, or to sexual stimulation with mating, without a minimal maintenance corticoid-treatment. These reactions are in fact not characteristic of the corticoids and could not be duplicated, in the absence of the specific stimulus, even with the highest doses of corticoids. The characteristic functional signs of A-C-overproduction which we see in the alarm reaction (e.g., atrophy of the lymphatic organs, catabolism, inhibition of inflammation) are also impeded by adrenalectomy and restored even by mere maintenance doses of A-Cs in the presence of stress, which sensitizes or "conditions" the tissues to them. However — unlike specific actions — these non-specific effects can also be duplicated in the absence of any stressor if large doses of A-Cs are given.

The importance of such conditioning influences is particularly striking in the regulation of stress-reactions, because, in the final analysis, they are the factors which can actually determine whether exposure to a stressor will be met by a physiologic adaptation syndrome, or cause "diseases of adaptation." Furthermore, in the latter instance, these conditioning factors can even determine the selective breakdown of one or the other organ. We are led to believe that differences in predisposition, due to such factors, might explain why the same kind of stressor can cause diverse types of "diseases of adaptation" in different individuals.

Incidentally, it was only on the basis of such experiments that the mechanism through which stress affects the adrenal cortex, could be clarified. We noted that stressors such as "formaldehyde, which caused marked adrenal hypertrophy in the normal, but not in the hypophysectomized animal, remained without effect (upon the adrenal), even if the adrenal cortex was prevented from undergoing atrophy by the administration of pituitary extract. The effect of such a drug on the adrenal appears to be an indirect one due to pituitary stimulation" (Selye and Collip, 1936).

*The concept of the L-A-S* — It had long been known that many local responses to injury are non-specific; it had been noted, for instance, that a variety of "topical stressors" (burns, microbes, drugs) share the power of producing non-specific tissue damage and/or inflammation. However, it is only recently that the close relationship between the systemic and local types of non-specific reactions has been more clearly established. While the characteristic response of the body to systemic stress is the G-A-S, characterized by manifold morphologic and functional changes throughout

the organism, topical stress elicits a "Local Adaptation Syndrome" (L-A-S), whose principal repercussions are confined to the immediate vicinity of the eliciting injury. They consist, on the one hand, of degeneration, atrophy and necrosis, on the other of inflammation, hypertrophy, hyperplasia, and, under certain conditions neoplasia.

*L-A-S and G-A-S* — At first sight, there appears to be no striking similarity between the systemic and the local reaction-type. A patient in traumatic shock furnishes a characteristic example of the G-A-S and, in particular, of its earliest stage, the "shock phase" of the general alarm reaction. An abcess, formed around a splinter of wood represents a typical example of the L-A-S and, in particular, of its "stage of resistance", during which the defensive inflammatory phenomena predominate. On the surface, these two instances of disease reveal no striking similarities and yet, more careful study shows them to be closely related.

The experimental observations which led us to these conclusions have been described elsewhere (Selye, 1953a, 1953b). Let us restate here, however, that, among other things, the G-A-S and the L-A-S are thought to be interrelated because:

(I) both are non-specific reactions, comprising damage and defense;
(II) both are triphasic, with typical signs of "crossed resistance" (or, depending upon the stressors used, "crossed sensitization"), during the second stage;
(III) both are singularly sensitive to the so-called "adaptive hormones" (ACTH, STH, corticoids);
(IV) if the two reactions develop simultaneously in the same individual, they greatly influence one another; that is, systemic stress markedly alters tissue-reactivity to local stress and *vice versa.*

*The concept of the Diseases of Adaptation* — Thus we arrived at the conclusion that the pathogenicity of many systemic and local stressor agents depends largely upon the function of the hypophysis-adreno-cortical system. The latter may either enhance or inhibit the body's defense reactions against stressors. We think that derailments of this adaptive mechanism are the principal factors in the production of certain maladies which we consider, therefore, to be essentially *Diseases of Adaptation.*

It must be kept in mind that such diseases of adaptation do not necessarily become manifest during exposure to stress. This is clearly demonstrated by the observation that temporary overdosage with desoxycorticosterone can initiate a self-sustaining hypertension, which eventually leads to death, long after hormone administration had been discontinued. Here, we speak of "metacorticoid" lesions. The possibility that a temporary excess of

endogenous aldosterone could induce similar delayed maladies deserves serious consideration.

Among the derailments of the G-A-S which may cause disease, the following are particularly important:

(1) An *absolute excess or deficiency* in the amount of adaptive hormones (e.g., corticoids, ACTH, STH) *produced* during stress.

(2) An absolute excess or deficiency in the amount of adaptive hormones *retained (or "fixed")* by their peripheral target organs during stress.

(3) A *disproportion* in the relative secretion (or fixation) during stress, of various antagonistic adaptive hormones (e.g., of ACTH and A-Cs, on the one hand, and of STH and P-Cs, on the other).

(4) Production by stress of metabolic derangements, which abnormally alter the *target organ's response* to adaptive hormones (through the phenomenon of "conditioning").

(5) Finally, we must not forget that, although the hypophysis-adrenal mechanism plays a prominent role in the G-A-S, *other organs* which participate in the latter (e.g., nervous system, liver, kidney) may also respond abnormally and become the cause of disease during adaptation to stress.

*Summary of observations* — To summarize we might say that all agents which act upon the body or any of its parts exert dual effects:

(1) *Specific actions,* with which we are not concerned in this review, except insofar as they modify the non-specific actions of the same agents.

(2) *Non-specific or stressor effects,* whose principal pathways (as far as we know them today) are illustrated in the adjacent drawing.

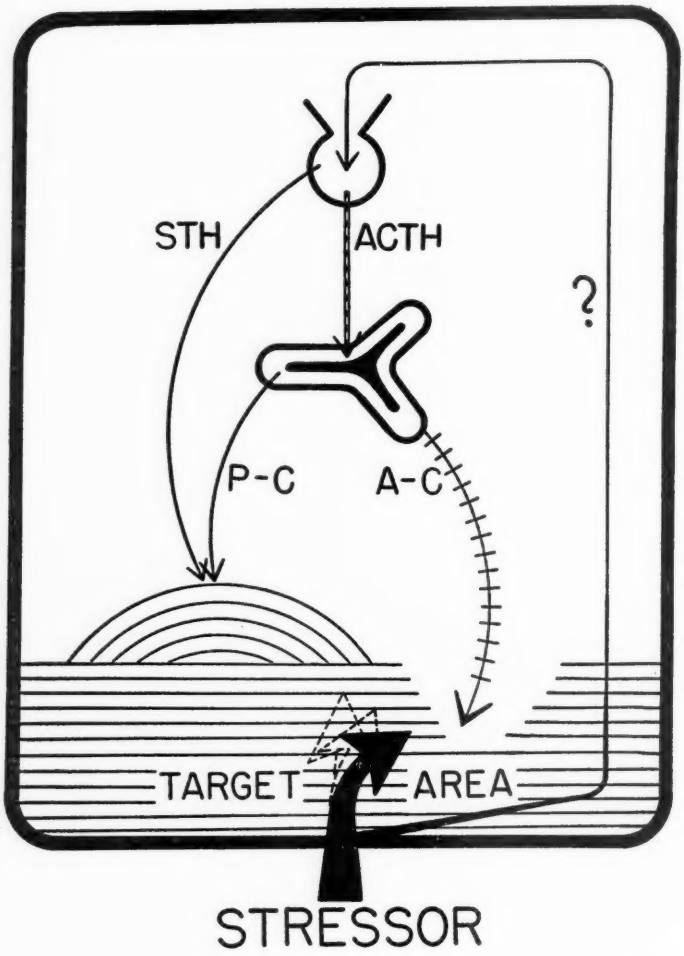
The *stressor* acts upon the target (the body or some part of it) directly (thick arrow) and indirectly through the pituitary and adrenal.

Through some *unknown pathway* (labelled by a question mark), the "first mediator" travels from the directly injured target area to the *anterior pituitary.* It notifies the latter that a condition of stress exists and thus induces it to discharge ACTH.

It is quite possible that this "first mediator" of hormonal defense is not always the same. In some instances, it may be an adrenaline discharge, in others a liberation of histamine-like toxic tissue metabolites, a nervous impulse or even a sudden deficiency in some vitally important body constituent (such as glucose or any enzyme).

ACTH stimulates the *adrenal cortex* to discharge corticoids. Some of these, the *prophlogistic corticoids* (*P-C*), stimulate the proliferative ability and reactivity of connective tissue; they enhance the "inflammatory potential". Thus, they help to put up a strong barricade of connective tissue

through which the body is protected against further invasion by the pathogenic stressor agent.




(After Selye, 1952.)

However, under ordinary conditions, ACTH stimulates the adrenal much more effectively to secrete *antiphlogistic corticoids (A-C)*. These inhibit the ability of the body to put up granulomatous barricades in the path of the invader; in fact, they tend to cause involution of connective tissue with a pronounced depression of the inflammatory potential. Thus they open the way to the spreading of infection.

It is not yet known whether ACTH always stimulates the adrenal to produce the various corticoids in the same proportion and always with a great predominance of A-Cs. Certain recent experiments (Hechter, 1953) suggest that, depending upon conditions, ACTH may cause the predominant secretion of one or the other of the steroid hormones. However, be this as it may, the *somatotrophic hormone* (STH) of the pituitary increases the inflammatory potential of connective tissue, very much as the P-Cs do; hence, it can sensitize the target area to the actions of the latter.

It is possible that the hypophysis also secretes some special corticotrophin which induces the adrenal to elaborate predominantly P-Cs; indeed, STH itself may possess such effects, but this has not yet been proven. In any event, even if ACTH were the only corticotrophin, the actions of the corticoids produced under its influence can be vastly different, depending upon "conditioning factors" (such as STH), which specifically sensitize the target area for one or the other type of corticoid action. Actually, conditioning factors could even alter the response to ACTH of the adrenal cortex itself, so that its cells would produce more A-Cs or P-Cs. Thus, during stress, one or the other type of effect can predominate.

*The fundamental reaction-pattern to topical stressors is a local adaptation syndrome with inflammation, to systemic stressors, the general adaptation syndrome. Various modifications of these two basic responses constitute the essence of most diseases.*

*Outlook suggested by these observations* — Pasteur, Koch, and their contemporaries introduced the concept of specificity into medicine, a concept which proved to be of the greatest heuristic value up to the present time. Each individual, well-defined disease, they held, has its own specific cause. It has been claimed by many that Pasteur failed to recognize the importance of the "terrain", being too preoccupied with the pathogen (micro-organism) itself. His work on induced immunity shows that this is incorrect. Indeed, allegedly at the end of his life he said: "le microbe n'est rien, le terrain est tout."

The theory which directed the most fruitful investigations of Pasteur and his followers was that the organism can develop specific adaptive reactions against individual pathogens and that by imitating and complementing these, whenever they are short of optimal, we can treat many of the diseases which are due to specific pathogens.

To our mind, the G-A-S represents, in a sense, the negative

counterpart, or mirror image, of this concept. It holds that many diseases have no single cause, no specific pathogen, but are largely due to non-specific stress, and to pathogenic situations which result from inappropriate responses to such non-specific stress.

Our blueprint of the pathways through which stress acts may be partly incorrect; it is certainly quite incomplete. But in it we have a basis for the objective scientific dissection of such time-honored, but hitherto rather vague, concepts as the role of "reactivity", "constitution and resistance" or "non-specific therapy", in the genesis and treatment of disease.

If we may venture a prediction, we would like to reiterate our opinion *that research on stress will be most fruitful if it is guided by the theory that we must learn to imitate — and if necessary to correct and complement — the body's own auto-pharmacologic efforts to combat the stress-factor in disease.*

*Acknowledgments*: Part of this work was supported by a Consolidated Grant from the National Research Council of Canada.

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PRESIDENT MONTGOMERY — We are indeed grateful to Dr. Selye for coming here today. As I said, he is a very busy person, and he has to go at two o'clock to a meeting in Windsor, where he is speaking again tonight. Thank you very much, sir, for coming here.

We now come to the Symposium on Coronary Artery Disease, and the lead-off man is Dr. J. Keith Gordon, Medical Director of the Sun Life Assurance Company of Canada who will begin our discussion on coronary artery disease. Dr. Gordon is well known to all of us, having been associated with the Sun Life for many years. During the last war he served in the Royal Canadian Army Medical Corps, being in charge of medicine in one of the Canadian hospitals overseas.

Prior to assuming full-time duties with the Sun Life, Dr. Gordon was Associate Professor of Medicine, McGill University, Montreal, and attending physician at the Montreal General Hospital. He is also a charter member of the Royal College of Physicians and Surgeons of Canada.

Dr. Gordon is going to review some old records from the Montreal General Hospital Department of Pathology which concern coronary artery disease.

We are very glad indeed to have Dr. Gordon here.

# CORONARY ARTERY DISEASE

A SYMPOSIUM

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The theory and practice of medicine is built on the foundation of past performances. "Only he who understands what has been can know what should be and what will be." It would seem, therefore, to be not inappropriate if I were to introduce this symposium on coronary thrombosis with a discussion of some phase of its natural history. History, however, embraces no more than a small part of reality, and on this premise I hope to escape the imputation that my data are insular in scope even though they consist of observations limited to the boundaries of one hospital.

In the Montreal General Hospital the first clinical diagnosis of coronary artery thrombosis with myocardial infarction was made in the year 1925. I remember the incident well. A medical student, aged 26, suffered a sudden seizure while attending a ward class and, because of the severity of his symptoms, he was admitted to hospital. A senior member of the attending staff in whose care he had been placed made a diagnosis of "coronary thrombosis", a term which was entirely novel to me in spite of the fact that Herrick's[1] classical description of the clinical features of the syndrome had appeared in the Journal of the American Medical Association thirteen years previously. "Death was now armed with a new terror."

During the years that have intervened since this incident I have repeatedly asked myself the question, as I expect many of you have, "Is the marked increase in the incidence of coronary artery thrombosis apparent or real?" If it is real, there arises the suspicion that an environmental factor may be involved in its production. Thus, this facet of the coronary problem may not be entirely academic. To quote the words of Paul White[2], "We need many more studies than we possess at present to determine to what

extent coronary disease, including coronary thrombosis, has been increasing, if at all, in the present generation." This statement, coming from the pen of an outstanding cardiologist, inspired Dr. Sydney Pedvis and me to make a search of the autopsy reports in the Central Division of the Montreal General Hospital from the year 1883 to 1944 inclusive. Case records from the year 1896 to 1944 were also explored. Our observations were confined to these two periods since no earlier autopsy reports were available and case records compiled prior to 1896 had been destroyed for lack of storage space. The study has since been projected to include the period from 1944 to 1953. The autopsy reports were reviewed in order to determine the ratio per cent of deaths from coronary artery thrombosis to the total number of autopsies. Case records were reviewed in order to determine the ratio per cent of patients to whom had been assigned a clinical diagnosis of coronary thrombosis to the total number of bed patients. The autopsy reports of the earlier years were given particular scrutiny for the purpose of establishing whether or not the pathologists who served the hospital during this epoch were aware of the implications of coronary artery thrombosis and its attendant morbid processes. It was observed that on inconspicuous occasions "occlusion of the coronary artery" was recorded. "Myomalacia cordis" and "softening", terms which were taken to indicate infarction of the heart muscle, were encountered with equivalent infrequency. Therefore, it is apparent that at least some of the pathologists laboring in this hospital have for a period of many years been aware of the fact that coronary artery thrombosis was one of the causes of death and that infarction of the heart muscle was an abnormality worth recording. In fact, in a summary of an autopsy performed by Wyatt Johnson on a 78 year old woman on February 28, 1886 these words appear: "thrombosis of coronary artery; myomalacia cordis; acute aneurysm of left ventricle; rupture into pericardium" — a perfect description of the sequence of events which occurs not uncommonly in this day and age.

While discussing this particular aspect of the subject with the present Pathologist to the Hospital, Dr. J. E. Pritchard, he drew my attention to an atlas of "Pathological Anatomy" produced by one J. A. Jeançon, M. D., and published by the Progress Publishing Company of Cincinnati in 1883. In the section which deals

with diseases of the heart and arteries there are very accurate descriptions, accompanied by coloured drawings, of "myomalacia cordis", mural thrombus formation and rupture of the heart. It may be of some significance that the author Dr. Jeançon makes no reference to the coronary arteries, and it can only be concluded that he was unaware of the fact that they were in any way implicated; nevertheless, our material was scrutinized with particular reference to "myomalacia cordis", mural thrombus formation and rupture of the heart and, as has already been stated, these phenomena were almost monotonously absent.

In order to go even further behind the scenes a review was made of the handwritten reports of autopsies which Sir William Osler performed while he was Pathologist to the Montreal General between the years 1878 and 1880, and which are now embalmed in the Osler Library, McGill University. Insofar as the heart is concerned, Osler's chief interest appeared to lie in the valves. He did, however, indicate that the coronary arteries were worth inspecting for in one of the autopsy reports this comment appears: "Posterior coronary artery which passes off behind this segment has a very small orifice, greatly contracted by atheromatous change. It only admits a probe about half a millimetre in diameter. Beyond this the artery appears of normal size and is not atheromatous. . . The orifice of the anterior coronary artery is a little contracted by atheroma. The artery itself is normal."

The infrequency with which these findings were recorded by the earlier pathologists, and in effect until the year 1933, when the curve begins to rise sharply, proffers considerable speculation. There is evidence to the effect that as early as 1886 one of the Hospital's pathologists was fully aware of the part played by the coronary arteries in the production of infarction and rupture of the heart, and it would appear highly unlikely that those who succeeded him would revert to a state of complete indifference toward these important anatomic structures. It is possible, however, that the coronary arteries were not dissected as a routine procedure. Infarction of the heart would have been patently obvious, but it is a secondary process which takes a little time to make its appearance, and if routine serial sections of the coronary arteries were omitted, it is more than likely that coronary artery

thrombosis without infarction may have been in many instances completely neglected. The suggestion may be made that the caliber of the pathologists was not of a high order. I can merely state that the post was held by such luminaries as Osler, J. George Adami (whose "Principles of Pathology" was the standard text-book of the English-speaking world in the early part of this century), Charles Warren Duval (who later became Professor of Pathology at Tulane University), and S. Burt Wolbach (who left the Montreal General to become Pathologist to the Peter Bent Brigham Hospital and Shattuck Professor of Pathology at Harvard). The quality of the autopsy reports in general shows that they were recorded by keen observers who were searching for the truth.

Incidentally, as a matter of historical interest, a page in one of the autopsy books contains this item penned by John McCrae when he was Pathologist to the Hospital in 1902 and 1903:

> "Here beginneth ye book of ye dead wherein is fayrely set forth ye last state of 417 persons that have departed this life; wherein be tabled diverse strange and fearsome conditions that led to ye same final end. God have them of his grace.
>
> Our life is but a winter's day;
> Some only breakfast and away;
> Others to dinner stay and are well fed.
> The oldest man but sups and goes to bed;
> Large is his debt, ye lingers out the day.
> He that goes soonest has the least to pay."

John McCrae became immortalized when, while on active service in the First World War, he wrote the poem "In Flanders' Fields".

Figure 1 shows the ratio per cent of coronary artery thrombosis with its associated phenomena found at autopsy to the total number of autopsies performed in the Hospital from the year 1883 to 1953 inclusive. While fewer autopsies were performed in the Hospital during the earlier years, it is to be noted that in the year 1916, when 383 autopsies were performed, there is no vestige of the finding of coronary thrombosis; also that in 1928, a record year for number of autopsies in the Hospital, only one discovery in 433 consecutive post-mortem examinations.

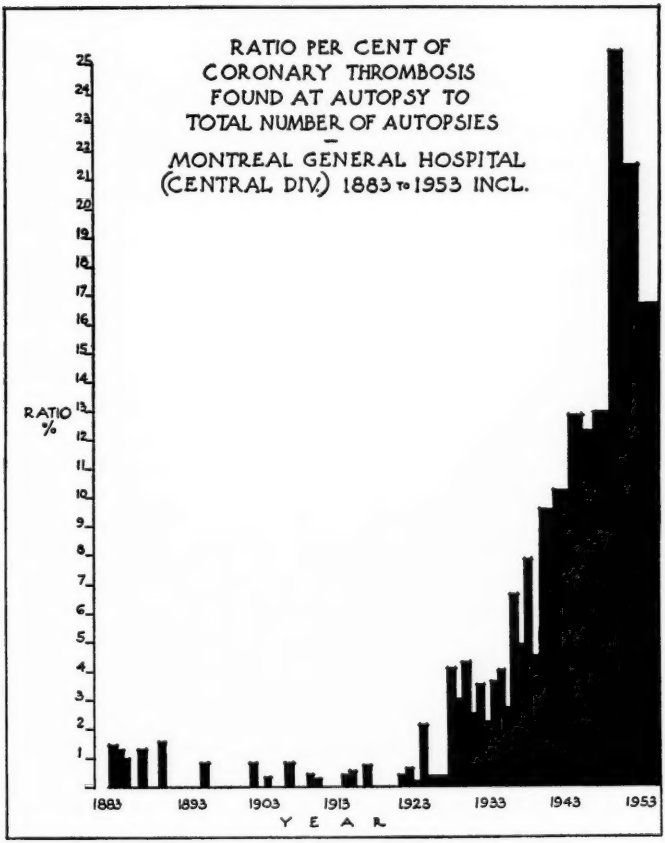


Figure 1

Figure 2 shows the ratio per cent of patients clinically diagnosed as coronary thrombosis to the total number of bed patients during the 1896-1953 period. This in graphic form portrays what would appear to be a phenomenon of the twentieth century.

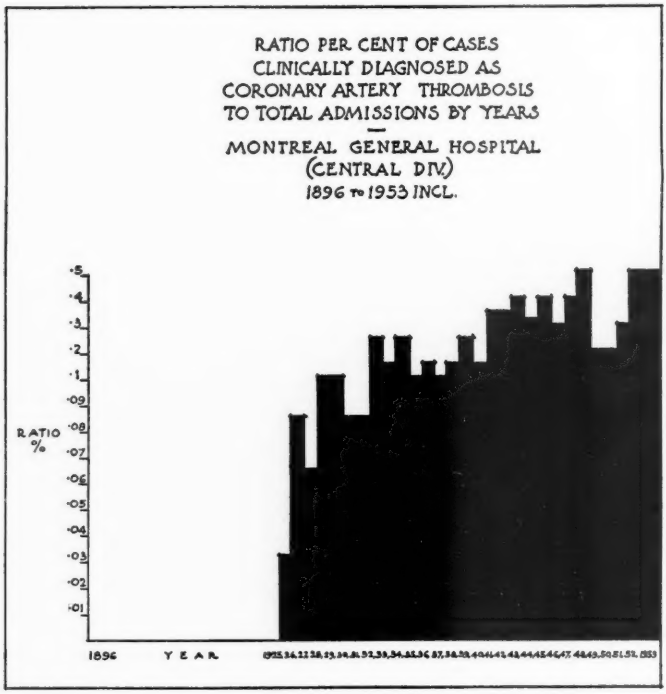


Figure 2

Figure 3 tends to corroborate what is already well known, that coronary thrombosis is more common in men than in women. In our series the ratio was approximately 4 to 1. It is also to be noted that the greatest number of deaths occurred in the group aged 50 to 59 years.

Refinements in diagnosis, a more coronary-artery-conscious medical profession, and the aging of our population are factors which have undoubtedly contributed to the startling increase in the number of deaths attributed to coronary heart disease; never-

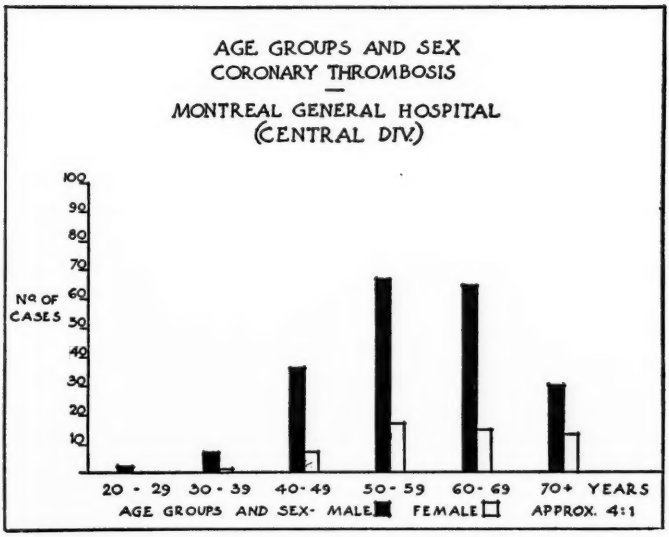


Figure 3

theless critical analysis of the autopsy reports from the year 1883 to the year 1953 and case records from the year 1896 to the year 1953 in the Montreal General Hospital casts some doubt on the validity of the hypothesis that we are dealing merely with a new aspect of an old problem.

(The author wishes to gratefully acknowledge the assistance given by Dr. Sydney Pedvis [1374 Sherbrooke Street West, Montreal] in the collection of the data.)

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PRESIDENT MONTGOMERY — Thank you, Dr. Gordon.

I think we will hold the questions until the three speakers have spoken, then we will get them all up here and they can decide which one will answer the questions that are proposed.

We will now have the second paper on coronary artery disease. This will be presented by Dr. Edward S. Mills, who is Physician-in-Chief, the Montreal General Hospital, and Professor of Medicine, McGill University, Montreal. He also has some interest in life insurance medicine, since he is Assistant Medical Director of the Prudential Assurance Company of England in their Canadian head office in Montreal. Dr. Mills will review the physiological and pathological backgrounds of coronary artery disease, draw attention to some of the clinical aspects, and comment on its importance in life insurance underwriting.

# CORONARY ARTERY DISEASE

A SYMPOSIUM

EDWARD S. MILLS, B.Sc., M.D., C.M., M.Sc., F.R.C.P.(C)
*Professor of Medicine, McGill University*
*Physician in Chief, Montreal General Hospital*
*Assistant Medical Director, Prudential Assurance Company Limited, Montreal, Quebec*

The growing importance of coronary artery disease as a killer is emphasized by the fact that today one in four Canadians die of it, many of them at a relatively early age. In the year 1939 the proportion was just half of what it is at present. The incidence has increased gradually since that time[1].

## PHYSIOLOGY AND PATHOLOGY

In order to refresh your memory concerning the background of coronary artery disease, let me review briefly the physiologic and pathologic changes which take place in the circulation to the myocardium.

During health and at rest the coronary artery flow is approximately 100–200 cc. per minute or 288 liters of blood per day. With violent effort and severe emotional strain this already voluminous flow may be increased tenfold, so that from one to two liters of blood are coursing through these vessels every minute — 2880 per day[2].

The control of this very active circulation under conditions of rest — emotion — or violent effort, rests with two sets of nerves — the vagus or parasympathetic which when stimulated forces the heart to go slower — lowers the blood pressure, decreases the cardiac output and in general reduces the work which must be done by the heart muscle; lessens its needs as regards the supply of food and oxygen and the removal of waste products. It is only natural therefore that stimulation of this nerve should reduce the flow through the coronary arteries by vasoconstriction. These effects are mediated locally by the liberation of acetylcholine.

In direct opposition to the vagus is the sympathetic nervous system which on stimulation increases the rate of the heart — raises the aortic blood pressure — increases the cardiac output and in

general puts an added load on the heart muscle. One might surmise therefore that an added effect would be dilatation of the coronary arteries with resultant increase in blood flow. This action is mediated by means of the liberation of adrenalin.

What happens, then, when arteries lose their elasticity or are partially occluded and no longer capable of responding to these nervous demands for dilatation and contraction. Under conditions of effort and strain the increased demands on the myocardium create a state of ischemia which is the cause of the pain in angina pectoris and the reason why the pain comes with effort or emotional strain and subsides gradually during rest.

For practical purposes, only two related degenerative processes are responsible for coronary artery disease — the first atheroma or atherosclerosis, a degenerative process involving chiefly the intima and resulting in narrowing of the lumen of the vessel. This condition would obviously seriously limit the blood flow through it — effectively preventing increased flow under conditions of strain. This disease may occur at any age; begins in adolescence and is often well marked in middle life especially in males.

The second, Monckeberg's medial sclerosis, is less serious since it affects principally the peripheral vessels and does not result in encroachment upon the lumen of the vessel though the artery is converted into a rigid tube. This is the condition which is so common in advanced age and which seldom affects younger age groups. Though lacking in elasticity the vessel's lumen remains relatively unchanged and hence it is less often a cause of angina pectoris than the other degenerative disease. These pathologic facts offer a partial explanation of why severe coronary artery disease is encountered in relatively young age groups with apparently labile vessels so far as one can judge whereas the more palpably damaged arteries are functionally more efficient.

On the basis of the foregoing physiologic changes, why is it that coronary occlusion often takes place during sleep or at rest?

The conditions which predispose to coronary occlusion are quite different from those which produce angina pectoris though the pain is likewise due to myocardial ischemia. Thrombosis, though occurring during rest, frequently follows a period of strain — with or without anginal pain. During this period as

has already been mentioned, sympathetic stimulation increases pulse rate — cardiac output and blood pressure — the narrowed coronary artery cannot cope with the demands and anginal pain results. With rest, the pain disappears, the pulse slows and the blood pressure falls. Now coronary flow depends in a great measure upon the blood pressure in the aorta at the mouths of the coronaries. With the fall in pressure during rest, the rate of flow drops — the blood stream in the vessels is slowed and at the site of one of the areas of narrowing in the artery, a clot forms — possibly aided by an unknown abnormal coagulation factor. Coronary circulation beyond the block is shut off and permanent myocardial ischemia results. In this connection it is pertinent to recall the now classical experiments of Cannon[3] who observed that a period of increased blood coagulability follows the outpouring of adrenalin during periods of emotional strain or effort. It would be of interest to know whether this change takes place in the human subject.

## THE RECOGNITION OF CORONARY ARTERY DISEASE

As medical directors of life assurance companies we have a special interest in two aspects of coronary artery disease. The first is — has the applicant significant coronary artery disease? The second is — if he has coronary artery disease, is he insurable and, if so, what is the risk in comparison with presumably healthy individuals in his age group?

### *A. The History*

To return to the first question — has the applicant coronary artery disease — let us break the problem down into its various components. The first is the history as recorded in the questionnaire and the most important single symptom is chest pain. But before discussing the importance of different types of chest pain, we must ask ourselves the question: Can coronary artery disease and/or occlusion occur without pain? The answer is yes. A review of the literature and an analysis of 220 cases by Roseman[4] indicate that about ten per cent of all instances of coronary occlusion occur without any pain whatsoever and this includes mere sensations of discomfort in the chest. It is presumed that in these instances the occlusion was gradual in onset.

If chest pain is admitted by the applicant what characteristics of the discomfort indicate that it is caused by disease of the coronary arteries?

Master[5] recently reported on an investigation of pain in 100 proven cases of coronary artery disease and in 100 individuals without proven heart disease. The patients were assessed on the basis of: 1) effort, 2) retrosternal location, 3) constriction or oppressive, 4) radiation to left shoulder or arm, 5) long duration, 6) no relief from nitroglycerin. His conclusions were that no single characteristic was a reliable guide but when three or more characteristics were present, a definite diagnosis could usually be made. In general, pain due to coronary artery disease whether angina pectoris or coronary occlusion is located retrosternally and not in the precordium. In angina pectoris it increases gradually during exercise or emotional strain and subsides rather promptly with rest — the whole process taking place over a very few minutes — usually less than a quarter of an hour. Coronary occlusion on the other hand is usually ushered in more dramatically and it remains until relieved by strong sedation. In both conditions the pain is characteristically of a compressing or squeezing quality and radiates to the neck and inner aspect of the left or both arms.

*B. The Physical Findings*

The physical findings often do not contribute much. The blood pressure may be normal — only one in four has hypertension. The heart is often normal in size and the heart sounds not remarkable. It has been shown that the state of the coronary arteries is comparable to those in the brain, the fundi and in the kidneys but not those in the periphery hence the best available guide is a thorough examination of the ocular fundi — unfortunately seldom if ever a requirement for life insurance examiners. It is to be hoped that an ophthalmoscopic report will soon become as routine as the blood pressure reading.

Another deficiency in examinations is the failure to determine the effect of effort on the cardiovascular system. It has already been stressed that many cases of coronary insufficiency will develop pain on evercise. Master's step test or some other form of exercise should, in doubtful cases, be part of the routine examination but avoided if other evidence points to coronary artery

disease. I well recall a middle aged man seen on a number of occasions over a period of 5 years because of chest pain on walking to the office. Many examinations failed to reveal the slightest evidence of organic disease. His heart appeared normal and the blood pressure 120/70. He admitted to an emotional apprehensive temperament and his wife stated flatly that the condition was "nerves". Finally one day I asked him to exercise in my consulting room in an effort to reproduce the pain. When I returned to the room it was unnecessary for him to tell me that the pain had appeared. His ruddy appearance had given away to pallor. He was sweating, apprehensive and when I took his blood pressure it was 210/120 although it had been normal 5 minutes before. Fortunately with a short rest the pain subsided, the color reappeared, the blood pressure returned to normal. During this entire episode the pulse remained at the 70 level.

*C. The Electrocardiogram*

The electrocardiogram can be and is of great value in supporting a clinical history suggestive of coronary artery disease, if it shows deviation from the normal pattern consistent with the suspected condition but it can be disappointingly normal even in the face of overt disease. Again exercise may bring out the latent abnormalities as in the case of Charbonneau, age 50, who was seen a year ago with angina of effort. Figures 1, 2 and 3 show a portion of the electrocardiograph in this case before, during and after the Master step test. I think you will agree that the one taken during the exercise is significant.

I need hardly remind you that Waldron and Constable[6] of the Mutual Life Insurance Company of New York after a careful statistical study said before this body in 1950: "We believe the results of this investigation indicate little or no significant correlation between the electrocardiograph and the ultimate prognosis".

*D. The Orthodiagram*

The orthodiagram also contributes materially in many cases but it may lead you down the garden path — to a wrong conclusion. I would remind you that an enlarged heart by x-ray measurement is usually one that is dilated and probably the seat of advanced disease. Prior to dilatation hypertrophy does not often

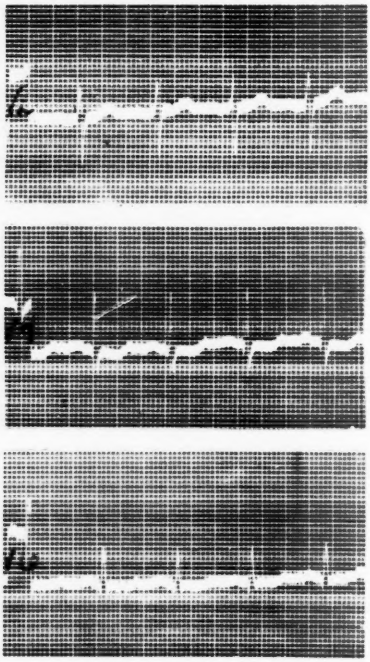

Figure 1 — Before Exercise

manifest itself by increase in the silhouette. Hearts weighing up to twice the normal may appear normal in the orthodiagram. This is a common observation.

In summary, therefore, the recognition of coronary artery disease depends, in many instances, upon a much more thorough investigation than is ordinarily carried out for life insurance purposes. A much more detailed history — particularly of chest pain or discomfort — a much more purposeful physical examination including the fundi and the effect of effort, coupled with what information may be obtained from the electrocardiogram and orthodiagram, are desirable in doubtful cases or where the assumed risk is for a sizeable amount. Unfortunately all investigations may at times fail to reveal even severe degrees of atheroma of the coronary arteries and the first indication of the

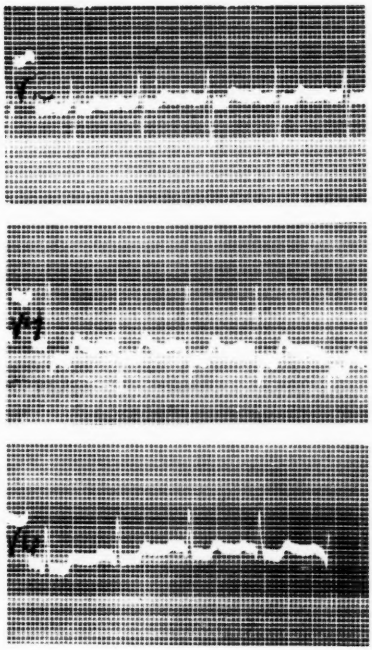

Figure 2 — During Exercise

condition may be sudden death.

## LIFE EXPECTANCY IN CORONARY ARTERY DISEASE

The second and equally difficult problem is the nature of the risk that the assurer takes when he accepts an individual with evidence of coronary artery disease. Is there any good yard stick for measuring the life span of such cases? I know of none. What factors, then, may influence the life expectancy of the individual with coronary artery disease. Here are a few.

*Age* — There is no valid proof that the younger the individual with coronary artery disease the better the prognosis other than the relative freedom of the younger groups from intercurrent disease. Schnur[7] who studied 399 cases of myocardial infarction concluded that age had little significance as regards prognosis. On the other hand, Stroud believes that closure of a coronary

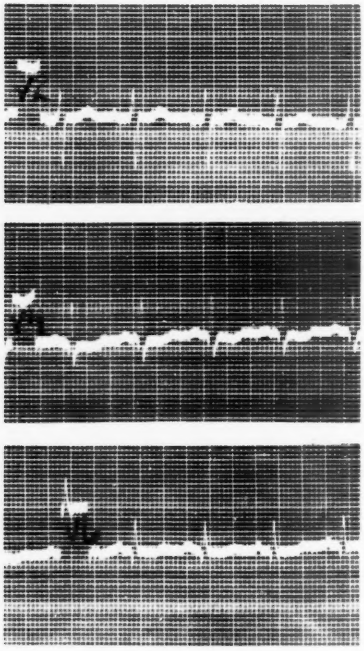

Figure 3 — After Exercise

artery in a young person carries with it a more serious prognosis.

*Severity of Attack* — All authors are agreed that the more severe the attack the poorer the prognosis. Russek and Zohman[8] in a recent analysis of 1318 patients' records compared 611 "good risk" with 707 "poor risk" cases. The mortality in the entire series was 33.8 per cent with only 3.4 per cent in the favorable and 60 per cent in the unfavorable group. To qualify for the "good risk" classifications none of the following criteria must have occurred: 1) previous infarction, 2) intractable pain, 3) persistence of shock, 4) cardiac enlargement, 5) gallop rhythm, 6) congestive failure, 7) cardiac irregularities, 8) other associated conditions such as diabetic acidosis, obesity, embolism, and others.

*Hypertension* — An elevated blood pressure adds materially to the mortality rate of patients with coronary artery disease.

*Occupation* — The cause of the increasing incidence of coronary artery disease as reflected in its complications such as myocardial infarction is of great importance to insurance carriers because it is increasing rapidly both in this country and in Great Britain, particularly in the male who is the heavy buyer of insurance. The following tables indicate: 1) the percentage of total claims in one company for the years 1946 and 1953 on account of the disease as compared with three other causes, 2) a comparison of the deaths from it in Canada for 3 years, 1939, 1944 and 1951 with deaths from other major causes, and 3) the incidence in relation to age and sex.

TABLE A

PERCENTAGE OF TOTAL CLAIMS

| | 1946 | 1953 |
|---|---|---|
| 1. Coronary Artery Disease and Thrombosis | 34.3% | 35.0% |
| 2. Cerebrovascular Disease | 1.6 | 7.0 |
| 3. Malignant Tumors | 23.1 | 30.0 |
| 4. Accidents | 26 | 14.8 |

TABLE B

THE MORTALITY IN RELATION TO CERTAIN OTHER DISEASES

| Arteriosclerosis of the | 1939 | 1944 | 1951 |
|---|---|---|---|
| Heart and Coronary Arteries | 15,762 | 25,853 | 31,133 |
| Cerebrovascular Disease | 4,788 | 9,089 | 12,880 |
| Malignant Tumors | 13,196 | 14,689 | 17,821 |
| Accidents | 6,071 | 6,845 | 8,034 |
| Total Deaths all Causes | 108,951 | 116,052 | 125,454 |
| Population | 11.3 M. | 11.9 M. | 14.0 M. |

TABLE C

MORTALITY FROM HEART AND CORONARY ARTERY DISEASE IN RELATION TO AGE AND SEX (1951) — (CANADA)

| | *Age* | *Number* |
|---|---|---|
| 1. Deaths from all causes | 45 – 64 | 27,540 |
| 2. Deaths from C.H.D. | 45 – 64 | 7,211 |
| 3. Deaths from C.H.D. males only | 45 – 64 | 5,632 |
| 4. Deaths from all causes males | 45 – 64 | 15,611 |

From these figures it is apparent that coronary artery disease as a cause of death is increasing rapidly and that many of these deaths occur not in the elderly, senile individual, but among men in the prime of life. One third of all deaths in men in Canada in the 45 – 64 year age group in the year 1951 was due to coronary artery disease.

Just to complete the picture, consider the death rate from coronary artery disease in relation to occupation — and to heavy buyers of life insurance. I have not been able to obtain figures for Canada but here are some from the British Isles:

Class 1 includes all types of professional men and business executives. Class 2 is mainly farmers; Class 3 includes clerks, hewers and getters, and various skilled workers such as foremen. Class 4 comprises partly skilled workers such as miners and Class 5 unskilled laborers of all types.

**TABLE D**

ARTERIOSCLEROTIC CORONARY ARTERY DISEASE
ENGLAND AND WALES
YEAR 1950

| *Class* | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Standard Mortality Rates | | | | | |
| Men 20 – 64 | 150 | 110 | 104 | 79 | 89 |
| All causes | 97 | 86 | 102 | 94 | 118 |
| Expected Deaths (no.) | 463 | 2428 | 6147 | 2245 | 2134 |
| Deaths Registered | 693 | 2668 | 6383 | 1778 | 1895 |

It is apparent from these figures that the standard mortality rates for members of Class 1 victims of coronary artery disease are considerably higher than for other classes but that for the year 1950 the actual registered deaths from this disease was 170 per cent. To come even closer to home, let me show you some figures dealing specifically with physicians — the first taken from statistics in the United States for the years 1938 to 1942[9].

TABLE E

CAUSE OF DEATH IN U.S.A. PER 100,000 POPULATION
1938 – 1942

| Age 25+ | Male Physicians | White Males |
|---|---|---|
| All causes | 2,052.6 | 2,022.1 |
| A. S. of heart and coronaries | 845.3 | 713.7 |
| Tumors | 198.4 | 244.5 |
| Accidents — Automobile | 44.2 | 49.5 |
| Other | 50.6 | 84.0 |

It is apparent that American physicians, while enjoying a favorable position with respect to tumors and accidents, are especially vulnerable to arteriosclerosis of the heart and coronary arteries. Standard Mortality Rates for physicians in England and Wales are from two to four times the rates for hairdressers and farmers judged by the following figures[10]:

In conclusion, it would appear not only that coronary artery disease is greatly on the increase throughout this country and the British Isles, but that this increase is mainly in professional men

TABLE F

STANDARD MORTALITY RATE FOR
ARTERIOSCLEROSIS OF HEART AND CORONARIES
IN PHYSICIANS ENGLAND AND WALES 1931

| | |
|---|---|
| Physicians | 368 |
| Hairdressers | 176 |
| Farmers | 68 |

and business executives. Both of these groups contribute very heavily to the total insurance issued and to an even greater extent to death claims. The time is surely at hand when underwriting committees must recognize this increasing hazard and take steps to adjust rates accordingly. Furthermore, it should be recognized that accepted procedures for determining accurately the insurability of individuals who have suffered from signs or symptoms suggesting atherosclerosis of the coronary arteries — with or without myocardial infarction — are far from satisfactory. The calculation of the nature of the risk by the insurer is to a great extent still a game of "actuarial roulette" rather than a carefully deter-

mined and known hazard. Time and experience with such risks will eventually provide the necessary information. In the meantime let us acknowledge the shortcomings of present methods of evaluating such risks and hope that newer and better methods of diagnosis and prognosis will pierce the veil of ignorance which hides the fate of the middle aged male with coronary artery disease.

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PRESIDENT MONTGOMERY — Gentlemen, we will now pass on to the third speaker in this Symposium on Coronary Artery Disease, which deals with an insurance point of view, and is to be given by Clifton L. Reeder, Medical Director of the Continental Assurance Company, Chicago. He is well known to all of us here. As the former papers dealt with the pathology and clinical viewpoint on coronary artery disease, it is felt necessary to have a discussion of the present insurance viewpoint concerning this subject. We are very glad, therefore, today to have Dr. Reeder tell us what the Continental Assurance Company is doing with people who have a history of coronary artery disease. He is also covering the subject of indefinite pain in the chest. Dr. Reeder indicated that he did not have sufficient material to give any statistical study, but he was persuaded to give us an idea of how his company handles this type of risk.

# CORONARY ARTERY DISEASE

A SYMPOSIUM

C. L. Reeder, M. D. *Medical Director,*
*Continental Assurance Company, Chicago, Ill.*

In 1948, Dr. Harry Dingman, with almost no assistance from me, decided that there must be some cases of coronary artery disease that could be insured on some basis. There were several factors which influenced his decision.

1 — Our Home Office staff attitude was emboldened with an immensely expanding business and all were looking for new horizons for our coverages.

2 — We had been experimenting with high substandard ratings for rheumatic heart disease and were enthusiastic about the possibility of adapting these ratings to other impairments formerly thought to be uninsurable.

3 — Coronary artery disease, particularly coronary occlusion with myocardial infarction, was being recognized more frequently.

4 — Clinically, by consultation with able cardiologists and in reviewing their statistics, it was obvious that more and more people were surviving the acute attacks and surviving longer than formerly.

With that background, it was immediately decided we could insure some of these cases on some basis. The problem was — on what basis? Both Dr. Dingman and I felt that we should be conservative in accepting these cases. We did not wish to commit the company to a large volume of business that might soon result in financial loss. Also, we wanted to feel our way along to see what underwriting problems we would encounter and how much of this business would turn out to be insurable.

Our criteria for acceptance were too rigid, which we knew at the time, but we did not know how to modify them with safety. They were:

1 — Onset before age 45

2 — Minimum of five years of complete recovery

3 — All electrocardiograms absolutely normal with the exception of Q waves in aVL and aVF, for at least three years prior to application
4 — All current physical findings normal
5 — Applicant working full time
6 — All applications limited to a maximum of ten thousand permanent insurance
7 — 500 per cent mortality ratio was assessed.

Frankly, we had no idea what would happen. We resolved that if we incurred a loss we could not lose much as long as a limited amount only was at risk on each applicant. There was also the possibility that our requirements were so rigid and the price so high that we would have no market. That would mean that the problem of selection against us would be very great. We told everyone our project was experimental underwriting. It was an experiment in insuring "uninsurables"; an experiment to see if high substandard ratings were practical. *Should a company do experimental underwriting?* My answer is an emphatic yes! We should continually try to broaden our coverages to include as many people as possible, even at some calculated risk to the company. It is a service we owe the public and our agents. Also it is very stimulating to Home Office personnel, especially to the Agency and Underwriting Departments.

In the beginning, the business came in slowly. We handled many trial inquiries trying to feel our way along. We quickly discovered that our original criteria were too rigid and gradually we relaxed them. We shortened the waiting period, increased the age limits, reduced the ratings as the recovery period lengthened and increased the amount we were willing to sell. Just how many policies were put in force I can only estimate, for our statistical file was not started until January, 1953, and was not working properly until later that year. Probably somewhere around 100 cases of coronary artery disease were in force by July, 1953.

From July 1, 1953 through August 31, 1954 we issued a total of 29 cases for $496,000 of insurance. This gives an average size policy of $17,000. Eleven policies for $182,000 were returned not taken. This means 18 policies for $314,000 were paid for.

The not-taken rate is 38 per cent by policy and 37 per cent by amount. This is high, but considering the price charged for the contracts it is not surprising. The ratings varied from 200 to 600 per cent mortality. The severity of the rating seemed to have no effect on the not-taken rate.

Altogether, I can estimate only that we have insured over 100 cases of known coronary occlusion. Since the beginning we have had only two death claims, one of which was "legitimate". I knew better at the time than to take the case but accepted it in a moment of weakness. The total premium on the case was high and I presume that influenced me. We collected two annual premiums before death. The second claim was an underwriting error. The case involved a physician and a bad examination after the usual preliminary trial papers. We learned a lesson from that one, and I do not think we shall be troubled with that type of loss again. Obviously, at this stage our mortality is excellent, too much so. But when will it go bad? Your guess is as good as mine and that is one reason why I prefer to be conservative in underwriting these cases.

Another factor in trying to qualify this type of case is the large number of trial inquiries that never end up with an issued policy. There must be at least three to four trials for every bona fide application and that represents a large amount of work.

Having started in the business of underwriting coronary disease we soon found ourselves underwriting all other kinds of heart abnormalities; Wolf-Parkinson-White syndrome, bundle branch block, wide QRS conduction, greatly prolonged P-R interval, T wave abnormalities, all kinds of tachycardia and fibrillation, and even anginal syndrome.

Accidentally, we saw one type of electrocardiographic abnormality of unusual interest because it was found in an individual who died the day after issuance of his policy. His only abnormality, if it is one, was an inverted T wave in lead aVF in the presence of a vertical heart.

The pattern intrigued me and I began watching for it. I also found the same abnormality could occur in the T in aVL in a horizontal heart. I discovered that Dr. Kirkland of the Prudential

was also interested — having noticed it in 1943. I expect that eventually it will be shown that these cases do have a definitely increased mortality hazard. Whether they are sole residuals of silent, or unadmitted, coronary occlusion or an indication of coronary artery disease or both, only time will tell.

As long as we were to cover as many of the aspects of coronary

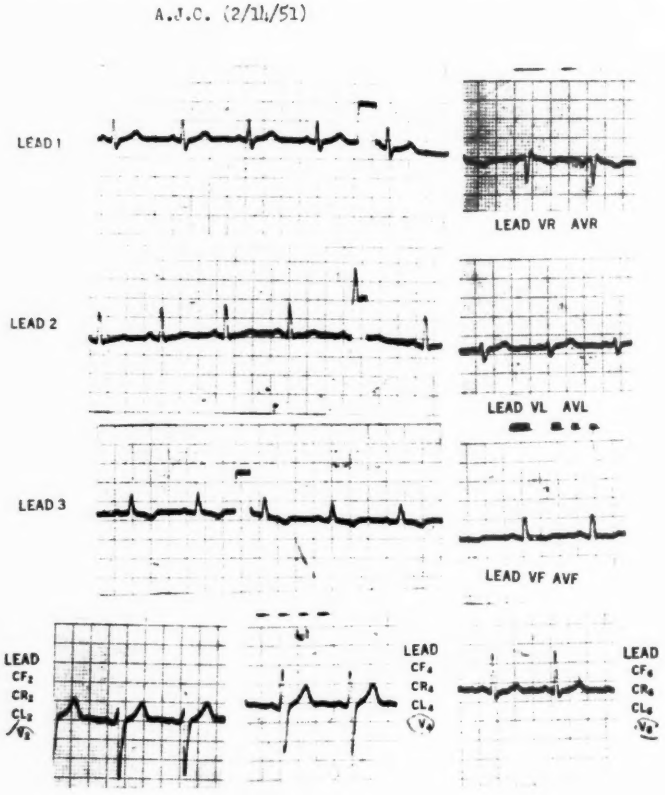


Fig. 1. A.J.O. Age 55. Medical history negative. Physical findings within normal limits. ECG considered normal by 3 companies. Note diphasic T in aVF in presence of vertical heart. Is this positional; residual of old, perhaps silent, coronary; or indication of coronary artery disease?

artery disease as possible Dr. Montgomery asked me to briefly discuss chest pain. Those of us who are actively underwriting every day have two types of cases continually plaguing us. One is that of labile blood pressure and the second is chest pain. The first is a subject unto itself. The second one is a troublesome problem and I did not realize how very difficult it was until I began to study our statistical file.

I will not bore you with all the various names and synonyms that go along with chest pain. We shall assume that we are concerned only with the undiagnosed cases of pain in the anterior left chest or substernal regions.

Of course, the underwriting in these cases is always a problem. What did he have? Are we getting the full story? Shall we send for the electrocardiograms? Shall we ask for a new one, perhaps with an exercise test? Does the size of the policy warrant our spending additional money to try and qualify the case? How im-

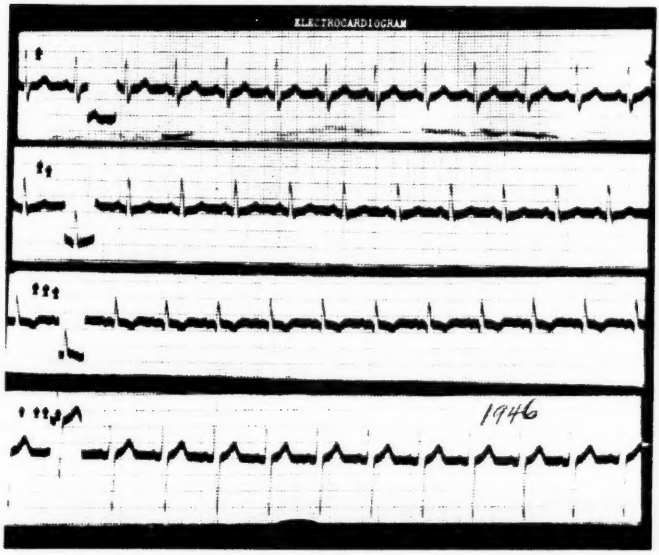


Fig. 2. A.J.O. Taken sometime in 1946. Tracing is same as one made 2/14/51.

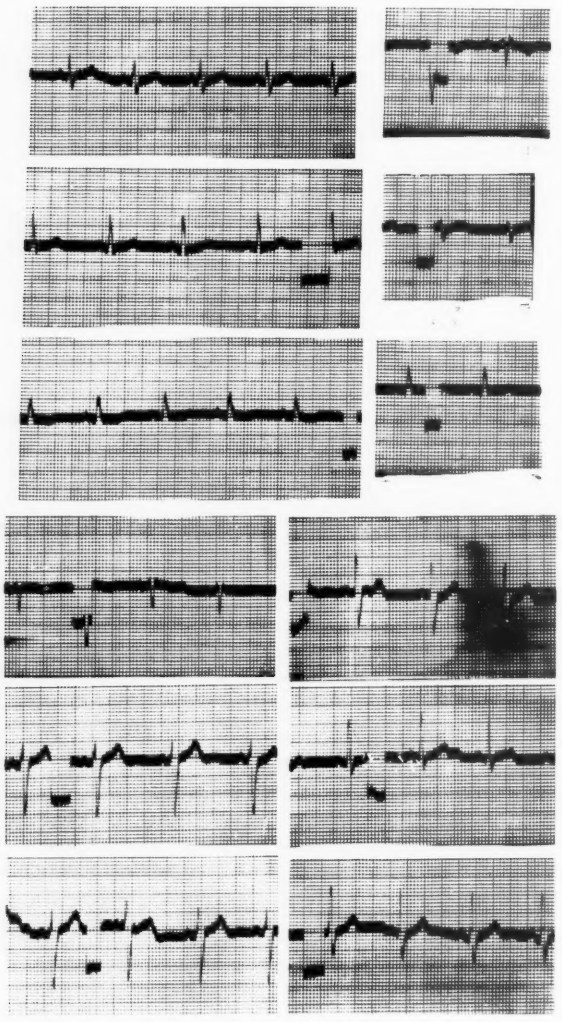

Fig. 3. A.J.O. Taken 8/17/50. Note $T_3$ now diphasic and T $aV_F$ is upright. Are these changes positional or additional proof of coronary insufficiency? The latter must be true considering that death from coronary occlusion occurred 6 months later.

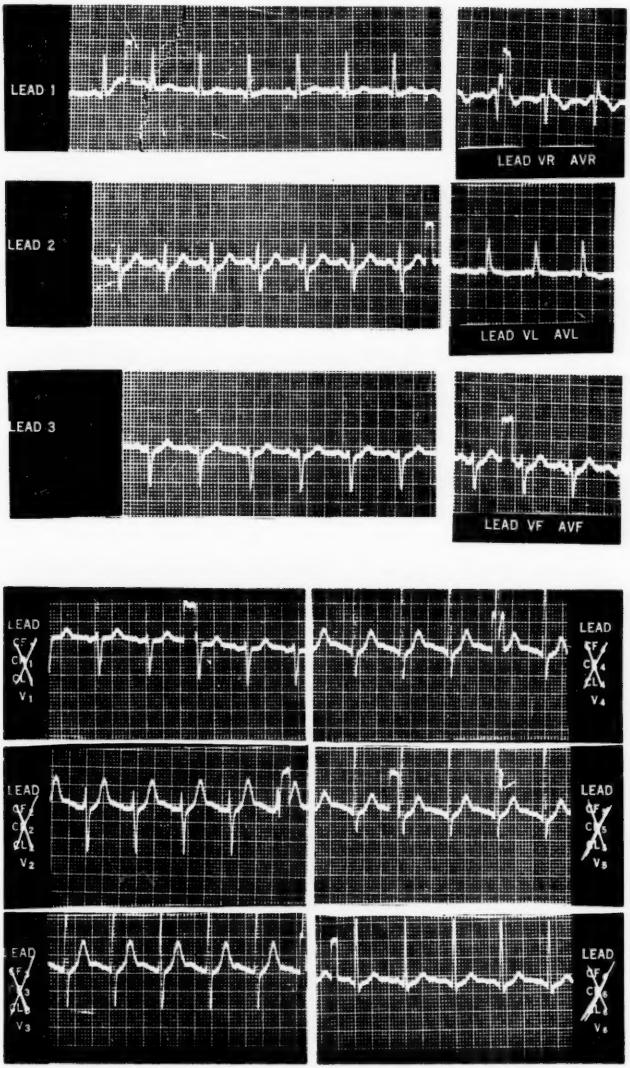


Fig. 4. D.A.M. Age 40. No history. Physical findings normal. Horizontal position. Note inverted T aVL. Positional or sign of coronary insufficiency?

portant is the agency aspect? What are the chances of placing a rated contract if one is issued? How do we start the sale of our underwriting decision to our agent? These are important practical questions that have to be decided.

With all the above questions in mind, we issued during the last six months of 1953 and the first eight months of 1954, 79 policies for $1,500,000 of insurance where chest pain entered into the underwriting. Thirty-five of these policies for $597,000 were returned not taken. Roughly 44 per cent by number of policies and 40 per cent by volume were not placed. All these cases were issued substandard. Thirty-seven were rated 150 per cent of which 20 were placed and 17 returned. Twenty were rated 200 per cent of which 9 were placed and 11 returned. The remaining 22 were rated 225 per cent or more. Of these 15 were placed and 7 returned. Please note that the more severely rated policies were accepted on a higher percentage basis than the others.

Gentlemen, these figures give me cause for concern. With such a high percentage of the policies being returned not taken, the question arises as to whether those who accepted are worse risks than we anticipated? That possibility is real. Why were so many returned? I suspect there was much discussion with personal physicians who, regardless of what they believed, were forced to tell their patients there was absolutely nothing wrong with them. Who is willing to buy a substandard contract when his own doctor says he is healthy? When I return to Chicago I intend to study each of these cases to see what further conclusions can be drawn. Until this time I had no idea that such a large percentage of these rated contracts were not accepted. I am very interested in hearing whether any of you have had the same experience.

In conclusion, we are very glad we entered the field of coronary disease in 1948. We expect to remain in it. There is not a great volume of this business that will be insurable. The cases that are accepted are expensive to handle — but in spite of the expense a very worthwhile investment. Needless to say, we must broaden our coverages to include as many people as possible. That is a duty which all of us accept when we become associated with the underwriting section of a life insurance company.

PRESIDENT MONTGOMERY — Gentlemen, I think we have heard

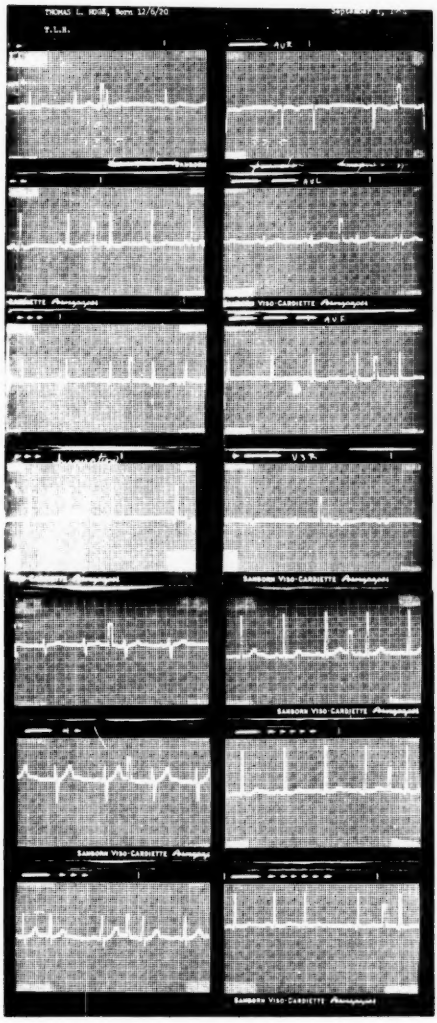

Fig. 5. T.L.H. Age 34. Premature auricular systoles in vertical heart. Note diphasic T aV$_F$. Again no medical history, no abnormal physical findings. Low T in V$_5$ and V$_6$, not unusual in vertical heart.

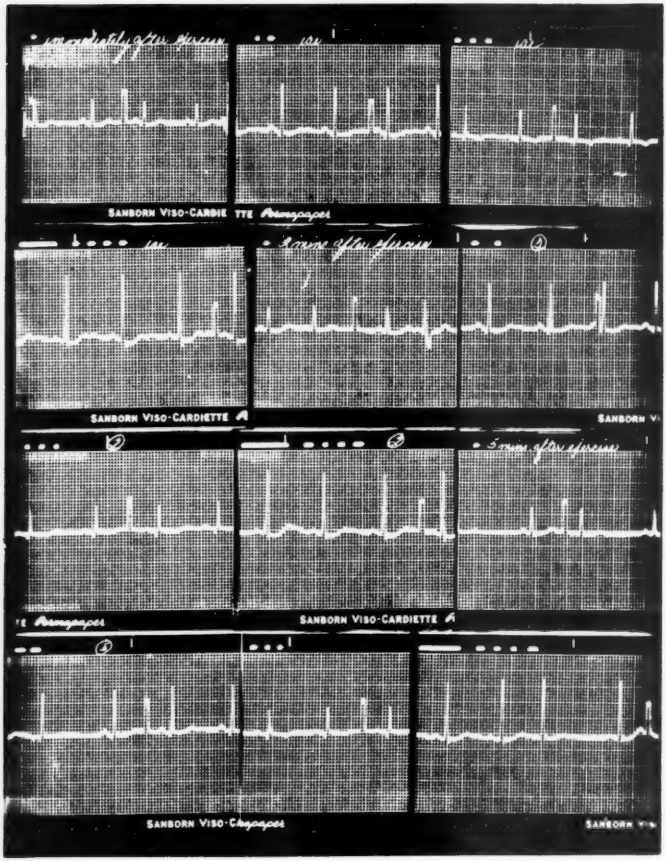


Fig. 6. T.L.H. Master's two step exercise test. Leads 1, 2, 3, and $V_4$ taken immediately after, 2 minutes after, and 5 minutes after exercise. Note S-T segment depression especially in $V_4$. Clinically, dyspnea was definitely increased. Test considered positive for coronary insufficiency.

three very interesting papers from the three doctors covering various aspects of coronary artery disease. I think there are some members now that have questions, so let us begin on them. Who wants the first question?

DR. GLADSTONE W. LOUGHEED — I certainly wish to congratulate Dr. Gordon, Dr. Mills, and Dr. Reeder on their excellent symposium. We all know that persons applying for insurance and giving a history of coronary episodes are increasing in number yearly.

Therefore, in order to insure this substandard group, I should like to ask Dr. Reeder how long a period should elapse after a coronary episode before you appraise the risk?

Secondly, also in cases of an applicant applying ten years after a coronary episode, can one be more lenient than if the episode occurred one or two years previously?

DR. REEDER — These points are very debatable, of course. When we started out originally, we wanted to be as conservative as possible, so we said that we would insist on a five-year period of recovery. We found that we limited the number of cases that we could accept if we did that, so we reduced the recovery period to a minimum of three years. Frankly, I am not so sure but what Dr. Montgomery and his group in the Manufacturers are correct when they say that they will take them after one year.

I base my opinion on personal experience of having underwritten practically every one of these cases that have come to Continental. Assuming you set up good criteria on which to accept them, the sooner you start collecting your money the better off you will be. I think if a man is over ten years away from his attack of occlusion, he is a better risk than if he is only one year or five years from it. That is our view in appraisal of these risks, and I think there are others who have also practiced that attitude.

PRESIDENT MONTGOMERY — Thank you, Dr. Reeder.

DR. FREDERICK R. BROWN — I understood Dr. Mills to say that he thought the abnormal electrocardiogram did not have any particular significance as to what is going to happen, but Dr. Reeder rather likes to have it return to nearly normal. I wonder if Dr. Mills would comment on that, and also tell us what he thinks about the prognosis of a case if the tracing returns very rapidly to normal, as opposed to that which takes two weeks to six months to return to normal.

DR. MILLS — Well, I hope I made it clear that the views that I expressed were the views of Waldron and Constable, of the Mutual Life of New York, who stated that as a result of their investigation, they could not give a prognosis on the basis of electrocardiogram alone.

DR. BROWN — I sort of thought I would like to get your opinion on it.

DR. MILLS — Well, I am not prepared to give such an opinion. In my undergraduate teaching at the University, I always emphasized the importance of not putting all your eggs in one basket, but to evaluate these cases on the basis of all the cases at hand, and I think we will go wrong less often if we take all of the evidence which is at our disposal into consideration in making up our mind, rather than to put too much emphasis on the EKG.

PRESIDENT MONTGOMERY — There is one point that I would like to make here. We assume, I take it, that this individual had an attack of coronary?

DR. BROWN — The previous year, yes.

PRESIDENT MONTGOMERY — So we know that he has had a coronary?

DR. BROWN — Yes.

PRESIDENT MONTGOMERY — Does that answer both of your questions?

DR. BROWN — Yes. I was interested in his idea about the prognostic significance of the electrocardiogram.

DR. REEDER — There is one comment I would like to make on this business of electrocardiographic changes which I feel rather strongly about, having seen quite a few of these cases. I have the very definite impression that the electrocardiogram has not returned to almost normal when there are remaining Q waves and there are variations in the S-T segment. I do not consider Q waves abnormal — I am speaking only of the S-T segment. Where there are deviations like that I feel there is an undue amount of coronary artery disease present. Now, whether I am correct or not only time will tell as we accumulate more and more of those figures, but that is certainly the way I feel about it right now.

DR. KENNETH F. BRANDON — First, of Dr. Mills, I would like to ask this. In selecting risks among middle-aged men, should one expect, and therefore should one search for more coronary disease, or should one search more carefully for coronary disease in cases admitting a history of, first, gout and secondly, gallstones?

The second question, if I may ask it now, is this. I would like to ask of Dr. Reeder this question. I assume that his cases are cases that have had an occlusion resulting in myocardial infarction. Of the cases that come to us we decide that this man may, or that man may not have coronary insufficiency. Now, if the key to the prognosis of coronary insufficiency is the collateral circulation, and this man who has not had an infarction is busy establishing a collateral circulation, as a group do you think they are better risks than Dr. Reeder's with healed infarcts?

DR. MILLS — I take it the first question was the relation of gout to coronary artery disease. I think we are all pretty well agreed that gout imposes a very considerable risk of coronary occlusion, that the incidence of coronary artery disease or the complications of coronary artery disease are much greater in the presence of chronic articular gout than they are in the individual who has never had gout.

The other part of the question has to do with the history of a middle aged man. Of course, I feel very strongly that the forms which I see in the company which I have the honor to represent are entirely inadequate in the matter of history. The question is asked, "Have you ever had chest pain?" and the applicant says, "No." However, if you were to sit down with that applicant for fifteen minutes and talk to him, you would probably find that he had indigestion, as all of us do at times, and it sometimes takes a little time to determine whether it is ordinary indigestion or whether it represents degrees of coronary insufficiency.

I think I mentioned in my talk that it was Master who pointed out that in order to get valid statistics he had to include those individuals who had just the vaguest retrosternal distress, who, in many cases, denied actual seizing retrosternal pain, but admitted to some pressure in the chest after emotional strain or exertion.

I am making a plea for a little more detail in the matter of his-

tory, so that we can determine better what we are dealing with.

DR. GORDON — I would just like to add something about that question of gout. I think that it is a most intriguing question. I am not speaking of chronic articular gout, but acute gout. I do not know whether a great many people with gout gravitated to me, but I seem to have seen more than my share of such patients when I was in practice — patients with acute gout.

Every one of those individuals, with the exception of two, are dead, and they died not very long afterward — within two or three years of their first attack of acute gout. They all died of coronary episodes.

Of the two that I can think of that are still alive, one has had multiple coronary episodes and is totally incapacitated, and the other one has had one coronary episode. So, I have got to the point where I look on acute gout simply as a manifestation of vascular disease.

PRESIDENT MONTGOMERY — Thank you, Dr. Mills and Dr. Gordon. Are there any other questions?

DR. REEDER — I would like to ask Dr. Gordon to give us some ideas as to the age breakdown on his patients that died. But, getting back to Dr. Brandon's question, of course the group that I read off were all known cases of coronary occlusion. There was no attempt to conceal anything on them. The problem was presented straightforwardly and we underwrote it straightforwardly.

We have tried halfheartedly and without any consistency to underwrite certain cases of coronary insufficiency. It has been strictly on a judgment basis. I can not give you any criterion for accepting them or rejecting them. When we have accepted them we have charged quite high mortality ratings.

I do feel that some of these things that show up in the electrocardiograms are not nearly as serious as they would seem to be. Fortunately, I have a company that so far has been willing to allow us to exercise our discretion and so far we have not violated their confidence by accepting large sums on these individuals. We do, therefore, have some control on them. I think from

the standpoint of underwriting stimulus, it is a desirable thing for all of us.

PRESIDENT MONTGOMERY — Any other questions?

DR. DAN Y. SAGE — I want to express my personal thanks to the speakers — present one question that may not be proper here, and what is the legal aspect of exercise before the electrocardiogram? If anyone has anything to say on that, I should like to hear it.

PRESIDENT MONTGOMERY — Did any of you gentlemen graduate in law?

DR. REEDER — I presented that same problem to our legal department and they all agreed that as long as the exercise test we require does not exceed the average or normal daily activity of a person by any undue amount, that there would be no legal liability as far as the company is concerned.

Now, when we do the test in our Home Office, we of course look at the electrocardiograms before we ask them to exercise. If there are abnormalities in the tracings we do not give the exercise test. How much reliance you can place on outside people doing that, I do not know. We have asked for such tests to be done outside, and expect to continue to ask for them outside. I feel that our legal liability is so remote that it is well worth while getting the tests.

PRESIDENT MONTGOMERY — Any other questions?

DR. EDSON E. GETMAN — I should like to ask Dr. Mills what his personal opinion is as to the value of the double Master's stress test — the negative double Master's stress test — in ruling on coronary insufficiency. In other words, will he put as much reliance on it as Dr. Master?

DR. MILLS — I take it the question is, if you do a double Master's stress test and it does not indicate a disease, what do you do then?

DR. GETMAN — That is right.

DR. MILLS — Well, I think it is a pretty good test. I do not think it rules out coronary insufficiency, but I would think that perhaps Dr. Reeder will make some money on these cases if he takes them on the basis of his present rates.

PRESIDENT MONTGOMERY — Any other questions?

DR. HARRY E. UNGERLEIDER — I would like Dr. Reeder, if he will, to again repeat his criteria for the acceptance of applicants who have healed coronary infarction. And, if I may, Mr. President, I would like to address the same question to you.

PRESIDENT MONTGOMERY — Dr. Breithaupt, have you got the answer? I contemplated listening to you.

DR. DAVID J. BREITHAUPT — Our impression was that we could take these people a year after the episode if they were fully recovered. We anticipated a mortality, perhaps, of 8 per cent per year, and we thought we would charge them accordingly. We had a dilemma of what to do with them after the time had elapsed, as has already been discussed this afternoon. We felt perhaps that some remuneration was worth while, and we told them that after five years we would come down some if they were still well, and after ten years we would come down further.

We feel perhaps that after ten years he is closer to the end of the rope, rather than improved, but we do not know. We do not have very much of this type of risk as yet.

I looked up our highly substandard risks the other day, and we have four cases of known coronaries, so we have no information to answer that question as yet.

PRESIDENT MONTGOMERY — Does that cover your question?

DR. UNGERLEIDER — You did not tell what your criteria were, except that the period was one year. You did not say anything about the electrocardiogram or anything else.

DR. BREITHAUPT — We do not feel that the cardiogram helps very much. It may be still somewhat abnormal. We avoid taking any arrhythmia. We think heart size is important. If it is enlarged, we do not want it. The blood pressure should be in a relatively normal range. He should be back at work and apparently well.

PRESIDENT MONTGOMERY — We have a special questionnaire we send out in which we ask the examiners to tell us how he is compared to a year previously, and I think Dr. Breithaupt did not mention that. We started this on the premise that these people,

on the average, will live seven or eight years, so therefore you have to get your money in.

DR. REEDER — I think that the single most important criterion for accepting these cases is their ability to return to useful employment, and return without any symptoms. Now, we have other criteria which we also use as well as that, but if we had to select the most important one, I think that is it.

Other criteria which I use in setting a price for this insurance are the rapidity with which the electrocardiogram returns to normal, whether or not there has been any pain subsequent to the alleged period of recovery, how long it took for this chap to recover. I do feel that it is important to know these things. You can go into a lot of minor things if you want, such as other history and other illness and work record and all that. They are all just things to look for but, most important to me, when I look at these cases, is whether he can work, and work without symptoms? Is he working because he has to or because he wants to? The second thing is, the appearance of the electrocardiogram currently, and how long it has been in as good a state as it is currently.

PRESIDENT MONTGOMERY — Unless there are any more pertinent questions, I think I will release these gentlemen. They have inadvertently coalesced into a panel, which I did not expect, for which I thank you, gentlemen. This was a very interesting subject, and I think it is worthwhile getting some of the thinking on it. It may not be the most important subject in underwriting, but it keeps us busy, anyway.

Our next speaker is Dr. Donald H. Woodhouse, Assistant Medical Director of the Sun Life Assurance Company of Canada. As well as being attached to the Sun Life Assurance Company, Dr. Woodhouse is clinical assistant in the Department of Medicine, Montreal General Hospital. While Dr. Woodhouse is a product of Western Ontario, having graduated from the University of Western Ontario, London, his post-graduate study was carried on in Montreal. He is a Fellow of the Royal College of Physicians, Canada. He will speak to us today on "A New Technic for Identifying Reducing Substances in the Urine."

# A NEW TECHNIC FOR IDENTIFYING REDUCING SUBSTANCES IN THE URINE: PAPER CHROMATOGRAPHY

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The title of this paper, namely "A New Technic for Identifying Reducing Substances in the Urine", requires some amplification. In the first place, it suggests that this paper deals with a laboratory procedure, and in this regard it is entirely correct. It also suggests that Paper Chromatography is a new technic, which is perhaps not entirely true. Although I am not aware of its having been used in life insurance medicine, it has become a fairly well known technic in medical and pharmaceutical work over the past ten years, and for many years has been used in industry for separation of dyestuffs, having been introduced in 1861. Because it can be easily applied to life insurance medical selection, we felt that a technic for its use should be published, if only to call attention to the fact that the technic of paper chromatography does exist. Methods now in use for the identification of urinary reducing substances are complicated, time-consuming and expensive, and for these reasons have not been widely accepted or used by insurance companies, despite the fact that such identification is often of considerable practical importance. Filter paper chromatography provides an accurate, simple and inexpensive means of answering an important question, namely, "Does a given urine, producing a positive Benedict's reaction, contain glucose?"

The theoretical aspects of paper chromatography are rather involved, and it serves no useful purpose to discuss them. The practical aspect of paper chromatography, in which our interest lies, is based on a very simple phenomenon. It consists of placing

a small amount of material on a limited area of a piece of filter paper, irrigating the paper with a solvent, and then, after the lapse of some time, applying methods for the identification of the material on the paper. Under suitable conditions the material will be found to have migrated from its point of application and, if a mixture, to have separated wholly or partially into its components. The procedure thus consists of two phases, namely the development phase, that is the irrigation of the material by a solvent, and the identification phase, which is the visualization of the material after migration by the application of reagents which produce colored areas in the positions occupied by the separated materials.

The distance that a specific substance will migrate under the influence of irrigation is expressed as the RF value of the substance, this value being the ratio of the distance travelled by the material to that travelled by the solvent front, measured from the point of application of the substance. In other words, a substance will migrate a distance that is specific for that substance when expressed in relation to the distance moved by the solvent front.

Although paper chromatography has been used to separate and identify many types of substances, we have been concerned with its use as a method of separating and identifying urinary sugars, and more specifically in its use in determining the presence or absence of glucose in urine. The technic we have been using, and which will be described, has been established in our laboratory by Dr. Guy E. Joron, of the Department of Metabolism of the Montreal General Hospital, who for several years now has been using paper chromatography as a technic for medical investigation in the field of metabolism.

Whatman No. 1 filter paper is used, being cut into strips six inches wide and eighteen inches long. A line is drawn across the paper three inches from one end, and it is on this line that the unknown substances are placed, thus assuring that all are at exactly the same level on the paper. On a paper of this size four unknown and one standard solution (for comparison) can be simultaneously run. Thus five quarter-inch spaces are marked off on the above line, one inch from each other. In the center of each of the four outer spaces the unknown urine specimens are applied, using a syringe and No. 27 hypodermic needle until the spaces are

filled. This is a convenient method of applying 1 microlitre of urine, since it has been found that this quantity of urine when applied to No. 1 Whatman paper forms a spot one-quarter inch in diameter. The same syringe may be used for each specimen to be applied provided it is thoroughly rinsed (8-10 times) in distilled water after each specimen. No foreign matter should touch the running portion of the paper due to the possibility of contamination. Note that the solution is applied to the spaces with the paper resting over a small open cardboard box so that both surfaces of this area of the paper are free from contact with any surface. A solution containing one per cent lactose, galactose, glucose and fructose is added to the center space, to act as control markers.

The paper is then placed in the apparatus. A variety of suitable cabinets can be obtained from the scientific instrument companies. In this laboratory a large pyrex jar twenty-four inches high and twelve inches in diameter, with a plate glass cover and rubber ring seal, is used. It is sufficiently airtight to allow the atmosphere within the jar to become at least partially saturated with the solvent used. We have found it useful to keep the jar constantly closed except when papers are being introduced or withdrawn, in order to maintain proper atmospheric saturation.

A stainless steel stand supports two glass troughs within the jar. The paper is held in the trough by folding it one inch from the end and weighing it down with a glass rod. The paper then runs over another glass rod, parallel and level with the trough and a short distance from it, permitting the suspended length of the paper to hang freely within the chamber.

Freshly prepared solvent, a pyridine-butanol-water mixture, is then added.

The lid is applied to the cabinet, and the whole apparatus is placed in a fume cabinet.

The solvent is allowed to run down the paper for from sixteen to twenty hours, a length of time that gives good separation of the sugars concerned.

The paper is now removed and allowed to dry by suspending it in a well ventilated cupboard or in a fume cabinet. When dry it is sprayed to saturation with the spraying reagent. A hand-operated

de Vilbiss non-corroding atomizer is suitable for the purpose. The paper is again allowed to dry.

The paper is then heated, either in an oven for ten minutes at 110° C. or directly over a hot-plate. Brown spots develop at the site of the sugar deposition, and the sugars may be identified by comparing the distance they have travelled with the markers. Note that the pentoses give a distinct pink color and may be accurately identified by running the pentose-containing specimen against a standard mixture of pentoses or individual known pentoses. The important sugars will be found to travel in the following order of increasing distance — lactose, galactose, glucose, fructose, arabinose, xylose and xyeloketose. The method is extremely sensitive, requiring only one microlitre of urine, and even in this volume glucose can be detected in a concentration of 0.1 per cent.

In analyzing the results of this technic the following data have been obtained, covering a period from March 1953 to August 1954 (18 months):—

9,876 urinalyses done
277 specimens (Benedict's or Clinitest) positive

Of the 277 specimens positive for a reducing substance, paper chromatography has yielded the following results:—

201 specimens revealed glucose
5 specimens revealed glucose and a second reducing substance (xylose in 4 cases, fructose in 1 case)
71 specimens revealed the reducing substance to be something other than glucose (xylose in 8 cases, fructose in 1 case, unidentified substances in 62 cases).

In short, approximately 25 per cent of the specimens revealed that the reducing agent was something other than glucose, and that no further investigation need be done toward excluding diabetes. This, I think, proves the practical value of the chromatography technic.

Further analysis of our results has allowed us to form other interesting and practical conclusions:—

(1) In the 71 specimens that did not contain glucose, all, with two exceptions, gave a quantitative analysis for urinary

reducing substances of 0.3 per cent or less. The two exceptions were one specimen revealing 0.5 per cent and one 0.7 per cent. One may thus conclude that if the quantitative reduction is greater than 0.3 per cent, it will almost invariably be found to be due to glucose.

(2) One cannot say, however, that the converse is true. Of the 201 specimens positive for glucose, 95 had a quantitative analysis of 0.3 per cent or less, indicating that even at these very low concentrations the majority of the specimens will contain glucose. For example, at a concentration of 0.3 per cent, 14 specimens contained glucose and 5 specimens did not contain glucose; and at a concentration of 0.25 per cent or less, 81 specimens contained glucose and 64 specimens did not.

It can thus be seen that it is with specimens that contain only traces of reducing substance that the technic of paper chromatography is of most value. It has been stated, and the opinion perhaps is widely held, that reductions of this amount are unimportant and can be disregarded. Yet our data would indicate otherwise. Over 50 per cent of such reductions are due to glucose and, as such, necessitate the exclusion of diabetes. It is of interest to note that in the cases showing glucose of 0.25 per cent quantity, we have been able to complete investigations on 58 (out of 81); 15 of these were proved to be diabetic, and two others were classed as potential diabetics.

It seems safe to conclude that urinary reducing substances, even in trace amounts, necessitate the exclusion of diabetes. In the cases to which we have applied the technic of paper chromatography, we have been able to immediately exclude diabetes in about 25 per cent of all cases, and the percentage rises to over 40 per cent in the cases showing reducing substances in trace amounts only.

It would perhaps make this presentation more complete if we had been able to accurately identify all the non-glucose reducing substances that have been present in the urines analyzed in our laboratory. This was, however, not possible and 62 urines remain classed as unidentified, meaning that the chromatographs were found to be blank on completion of the chromatography technic.

Most of these unidentified specimens were subjected to further chromatography analysis in the Department of Metabolism of the Montreal General Hospital by Dr. Joron, using a variety of developing solvents and sprays. In many instances the cause of the reduction has been identified, and after a much longer series is completed it is likely that Dr. Joron will report his results elsewhere. Many different substances which are known to be reducing agents have been identified in these specimens, such as salicylates, creatinine and ascorbic acid and its degradation products. In some of the specimens the conclusion reached was that many different substances present in infinitesimal amounts were acting jointly to produce the reduction. It is the hope that continuation of these analyses might eventually result in the development of useful data, but at present little more than this can be said.

*Appendix*:—

Reagents:—All chemicals are of analytical reagent grade.

(1) Running solvent (pyridine-butanol-water mixture):—15 ml. N-butanol, 5 ml. pyridine and 7.5 ml. distilled water are mixed in a separating funnel by inverting (violent agitation will delay separation). Two layers form, the bottom of which is run off and placed in the bottom of the apparatus jar. Five ml. pyridine are added to the top layer, which is agitated, and then placed in the trough. The solvent should be prepared shortly before each run.

(2) Spraying reagent:—3 gm. stannous chloride, 1.25 gm. p-phenylene diamine, 200 ml. absolute ethanol, 50 ml. glacial acetic acid. The solids are weighed accurately and added to the liquids, mixed, left to stand for 30 minutes and filtered. The solution is yellow at first and shortly turns pink mauve before using. The solution keeps for one month, stored in a refrigerator.

PRESIDENT MONTGOMERY — We have had a very interesting paper of an unusual type. Are there any questions you want to ask Dr. Woodhouse?

DR. J. RANDOLF BEARD — I would like to ask about the apparatus itself. Is that available that way, or did you have it made up? I would also like to have some idea of the cost, that is, the

jar and the top with the seal on it, the stainless steel stand, and that part of it.

DR. WOODHOUSE — We improvised a bit on our apparatus. They are available in all the equipment houses; they all have apparatus such as this, apparatus that has been designed for this chromatographic technic. This is one that we ourselves dreamed up. We had the jars and somebody sawed the top out of an old casting; but you can buy those all made up.

DR. BEARD — Do you know about what the price of that runs? That is always a question when it comes to laboratory work.

DR. WOODHOUSE — Well, I am not sure. I would think the total cost of our equipment perhaps came to $30. I would think you could buy it all made up for $100 or $150. I am just guessing, though.

DR. RUSSELL W. ZINKANN — Dr. Woodhouse, do preservatives interfere with the test in any way?

DR. WOODHOUSE — No, nothing interferes with it. You see, the solutions, the salts, and the sprays have all been designed to identify only sugars. Our identifying reagents and solvents are such that we will only identify sugars. We have found no interference of any kind, and that is why we do not show up the salicylates or anything else that may be in there. This technic is designed to show just one thing — is there glucose present or not? From our standpoint it is rather academic, if there is not.

QUESTION — Has this test helped to alleviate blood sugar studies? Have you found any advantage there?

DR. WOODHOUSE — Well, I had hoped that I had made that clearer. We feel that getting additional urines after you have a positive is more or less a waste of time, and we almost immediately go back for a glucose tolerance curve. Prior to the introduction of this, all these people — the 25 per cent that turned out not to have glucose — all would have had a glucose tolerance curve or some form of investigation to exclude diabetes. On obtaining the information that the substance in the urine is not glucose, we have dispensed with all further investigation.

QUESTION — What advantage, if any, would that have over fermentation?

DR. WOODHOUSE — Well, I am not an authority on fermentation. To us, the value of this technic is its simplicity. It involves no labor. I do not know whether fermentation does or not.

PRESIDENT MONTGOMERY — Thank you, Dr. Woodhouse.

Our speaker now is Dr. Harry Botterell, Associate Professor of Surgery, University of Toronto. He is the Senior Neurological Surgeon at the Toronto General Hospital.

Dr. Botterell is from the West, having graduated in 1930 from the Medical School in Winnipeg. Following graduation, he spent the next six or seven years in becoming proficient, not only in neurology but also in general surgery. He is internationally trained, spending time in Toronto, Montreal, Johns Hopkins, Yale and Queen's Square, London, England. During the war he was the senior surgeon in the Canadian Neurological and Plastic Surgery Hospital when hostilities were at their height. He spent over four years in the Royal Canadian Army Medical Corps.

Dr. Botterell is one of those rare people — a fertile mind and boundless energy. Today we are honored to have him speak to us on "Neurosurgery Today and Tomorrow."

# NEUROSURGERY TODAY AND TOMORROW

E. Harry Botterell, O.B.E., M.D., M.S., F.R.C.S.(C)
*Associate Professor of Surgery*
*University of Toronto*

It is my impression that countless numbers of books and papers review at frequent intervals the status of neurosurgery today, and what is hoped from it tomorrow, and what relation it has to your responsibilities. Therefore, it seemed to me to be of the maximum potential interest if I reviewed what we are doing in the University of Toronto and what seems of particular interest elsewhere.

The preparation of this paper has required close scrutiny of the activities of the neurosurgical unit of the Toronto General Hospital to allow reasoned comment about neurosurgery today. For two and a half months, during the spring and early summer of 1954, I was able to visit my colleagues in Britain, and one of my objectives was to formulate plans for research and discussion with my colleagues bearing on the neurosurgery of tomorrow.

By virtue of the relatively small number of neurosurgical cases passing through even a busy neurosurgical unit, it is probably safe to conclude that medical directors of great insurance companies have little direct contact with neurosurgical problems, and may even eschew accepting the occasional particular problem case, either for insurance or as an annuitant. May I claim the age-old privilege of the practicing physician or surgeon and tell you of a case I had? My commanding officer in World War II at the time of the Canadian raid on Dieppe expressed great interest in finding out what really went on when neurosurgeons dealt with penetrating brain wounds. He, I infer, having come from a general hospital, had not a little skepticism about the never-ending demands of neurosurgeons for arrangements other than those usually provided for surgery in an Army hospital in time of war.

Patient D. J. was admitted three days following a penetrating wound from a high-velocity missile which entered the left parieto-occipital region and emerged in the left frontal-temporal region.

By the time the damaged brain to the depth of an inch had been exposed and all damaged tissue had been removed, two and a half to three hours had passed. My assistant, my commanding officer, and, gentlemen, your President, had a good deal of fatigue, fallen arches, and a great deal of newly-replenished sympathy for neurosurgeons.

May I add in passing that Dr. Montgomery's contribution to the Canadian Neurological Hospital, the neurosurgical base of the Canadian Army overseas, played a most important part in the development of that hospital.

This patient, for whom Dr. Montgomery and I take joint responsibility, has made a great recovery from a total global aphasia resulting from this wound, and by tremendous perseverance has re-educated himself in his capacity to speak, to read, and to write, although there is still a definite deficit. In spite of this, he has become a buyer in a large departmental store in Regina, purchasing about $400,000 worth of ladies' hose each year. I should say that his prognosis is a good one. He has had but two minor epileptic seizures in fourteen years, and I see no reason why this brain wound should shorten his life.

*Brain Injury* — It is a fact that the majority of penetrating brain wounds, both civilian and military, make such recoveries, excepting for the incidence of epilepsy, which occurs in between one-third and one-half of all cases.

Cranio-cerebral injuries are a widespread problem. The prevalence of high-velocity transportation is accompanied by a large number of head injuries. Munro has said that the frequency of serious head injuries resulting from motor vehicle accidents bears a direct proportion to the velocity or speed of the transportation.

For the most part, the uncomplicated closed head injury is managed in the first hospital to which the patient is admitted. Head injuries complicated by penetrating brain wounds and intracranial clots can be transferred to neurosurgical centers for special investigation and operation.

Young and middle-aged adults withstand a serious head injury surprisingly well, and even after a period of unconsciousness with post-traumatic amnesia of days, they have a good prognosis.

Should the brain injury be associated with an unusually long period of unconsciousness and post-traumatic amnesia, and result in deterioration mentally and emotionally, the patient's prognosis is bad.

Penetrating brain wounds and intracerebral clots requiring evacuation carry a risk of post-traumatic epilepsy ranging from 33⅓ per cent to 50 per cent in various authors' follow-up studies. The incidence of post-traumatic epilepsy is very low following a closed head injury without a penetrating brain wound and with but momentary or short periods of unconsciousness and post-traumatic amnesia. It is probably of the order of 2 per cent to 5 per cent in the more severe closed head injuries.

A review of the work done by our unit in the Toronto General Hospital during a six month period shows that we are dealing with complicated brain injury cases transferred from other centers, a few brain abscesses in spite of all the antibiotics and sulfa drugs, 71 brain tumors, 14 cerebral aneurisms (a post-war development), and 58 herniated discs — we did more brain tumors than discs in that period. Also, intractable pain from cancer, and other causes accounted for 38 cases, and there were 50 miscellaneous patients.

*Spinal Cord Injury* — I now wish to turn to spinal cord injuries. These constitute the second great form of trauma of the nervous system. In each war there has been a grim harvest of transverse myelitis, or paraplegia, following disruption of the spinal cord.

In time of peace each year in Ontario, diving into shallow water produces a score of patients with fracture dislocations of the cervical spine, and destruction of the spinal cord. Highway accidents, accidents in the forests, construction camps, and mines are responsible for a group of comparable size of fracture dislocations in the thoracolumbar region with destruction of the spinal cord. Today, these patients no longer die in the months following injury.

In Britain, the United States, and Canada, prompt transfer of these patients to neurosurgical units especially set up to deal with the problems of acute spinal cord injury, the availability of sulfonamides and antibiotics to control the infection, and the establishment of rehabilitation centers for paraplegic patients have greatly

reduced the mortality in the first decade following injury. These patients return to their homes, and many of them engage in useful occupations. Among such a group of 103 war veterans injured between 1940 and 1945 there have been 25 deaths. They were the usual Army age group, from 21 or 22 to 31 or 32 at the time of their injury. It is only fair to point out that several of these patients, following the trials of evacuation from France to Canada, were grievously ill on their arrival in Toronto, and two or three died within the first two weeks.

A comparable group was investigated among the Workmen's Compensation Board cases treated by the same team which developed the paraplegic center for veterans in the years following the war. In that group there has been a very low mortality rate in the patients promptly evacuated to a paraplegic center from all over Ontario and coming under treatment before the development of complications.

There is a very tough problem which one is asked about: How long do you think a paraplegic patient will live? My colleague, Dr. Albin Jousse, who directs the program and institution responsible for the rehabilitation of these patients, has summarized the over-all results of treatment. In patients with varying degrees of cervical cord transection in the hospital, there are six unemployed and four working in the veterans' unit. Out of the hospital, there are seven unemployed and ten employed at some form of gainful labor. These patients are living at home, of course, with assistance from their families.

You are all familiar with the quadraplegic who has little use of his arms, and none of his legs or trunk, with bladder and bowels paralyzed. There has been remarkable improvement in the survival of patients with complete or incomplete destruction of the spinal cord in the thoracolumbar region. The survival of these patients is an achievement — a urological accomplishment — of the first order, led by Dr. Carl Aberhart. We must hope that at the end of another decade the majority of these patients, who have almost reached the status of colleagues, will be here collaborating in our researches into these problems of spinal man. The most superficial contact with these men and women inspires the thought

that prevention of diving accidents and industrial accidents is the paramount problem.

In this direction, the Workmen's Compensation Board of Ontario and the Federal Department of Labor have been most active, and are in process of making a documentary short film emphasizing the need for prevention and proper methods of transporting these patients with back injuries.

It is a terrible thing to have a patient able to move her legs and arms after an accident, only to find that by the time she gets to the x-ray table she is paralyzed.

*Intra-cranial Sepsis* — The medical history of intracranial sepsis, secondary to infection in the ear or mastoid, paranasal sinuses, penetrating brain wounds or pulmonary sepsis, may be divided into the eras before and after sulfonamides and antibiotics. My chief, Dr. K. G. McKenzie, the founder of the Neurosurgical Service at the Toronto General Hospital, and indeed the first neurosurgeon in Canada, analyzed the over-all mortality rate of brain abscesses in the Toronto General Hospital before sulfonamides and antibiotics, and found it to be 50 per cent. This was in keeping with the experience in other neurosurgical centers during that era. A similar analysis carried out during the last decade has shown a mortality reduced to 15 per cent, and save for human fallibility it would have been below 10 per cent.

A brain abscess kills either by forming an intolerably large space-occupying lesion, or by spread of infection, with resultant ventriculitis and meningitis. Before antibiotics, every operation was subject to this hazard. Today, unless the brain abscess is in a particularly vulnerable part of the brain, the lesion can be extirpated and the spread of infection prevented.

Here is a picture* of a brain abscess in the frontal region, secondary to frontal sinus infection. It is an encapsulated abscess. It was removed, and ruptured in the process and the patient made a good recovery.

Here is an abscess* which has been completely removed, and

*Lantern slide photographs were used to illustrate the subject material. — Ed.

there it is split. Systemic and local application of antibiotics prevented infection, and the patient made an uneventful recovery. This patient has remained well for the past six years. I am satisfied that successful radical excision of the infective process and elimination of the primary focus gives these patients a good prognosis over the long term, save that the incidence of epilepsy is of the same order as in penetrating brain wounds, that is, about one-third to one-half of the cases where the lesion is situated in the frontal lobe, with a lower incidence in the temporal lobe abscess and no epilepsy following extirpation of an abscess from the cerebellum.

Brain abscesses used to keep surgeons awake at night, and now we really almost welcome brain abscesses, because one is so often able to extirpate cleanly the lesion and deal with the primary focus. Provided another abscess was not left behind, these patients do well.

*Brain Tumors* — Brain tumors, however, are a much less happy story and have been a problem difficult of solution since the era of Sir Victor Horsley, whom Horrax so rightly describes as the father of neurological surgery. Benign or malignant as the tumor may be, the fact that it is an expanding, space-filling lesion makes certain a fatal termination.

Infiltrating gliomas must be judged malignant, though they rarely metastasize. Local recurrence and spread of the tumor is the rule, and radical, apparently complete removal fails to effect cure. Relief of intolerable headaches and preservation of useful and happy lives for limited periods are achieved in a significantly high percentage of patients with cerebral gliomata, constituting a not altogether unsatisfactory result to patient, relatives, and surgeon.

The shining exception to this gloomy picture of gliomas, about 40 per cent of the intracranial tumors coming to operation, is the cystic astrocytoma of the cerebellum. In this group of cases, where the nubbin in the wall of the cyst can be completely removed, many patients operated upon for the most part in childhood or young adult life have lived for many years. There is a major biological difference between all other gliomas and cystic gliomas of the cerebellum.

The site of the glioma and its inherent degree of malignancy are the factors controlling operability and the survival period.

X-radiation of increasingly high voltage, cobalt 60 irradiation, the local use of isotopes, are some of the current physical methods of treating inoperable gliomas, and of complementing surgical treatment.

Gliomas of the brain are the bronchogenic carcinoma of the pulmonary surgeon and the gastric carcinoma of the abdominal surgeon, and represent the same problem. In our center, my colleague, Dr. Tom Morley, has begun a study of tissue cultures of brain tumors supported by a grant from the Ontario Cancer Research Foundation, seeking to further our understanding of the biological qualities of gliomata and the effects of physical, chemical, and biochemical agents upon these tumor tissue cultures. Certainly we have carried the radical exterpation by technical means about as far as it can be carried.

Meningiomas (dural endotheliomas), are benign tumors in that they do not metastasize, and if completely removed, the patient should remain well. Their slow growth allows them, in many instances, to attain a large size before overwhelming the brain's capacity to compensate for a space-filling lesion. There occurs a great vascularity of the overlying structures, the skull, dura, and scalp. While they may occur anywhere within the cranium, they have a predilection for the region of large venous sinuses, such as the sagittal sinus, the lateral sinus, and for the region of the carotid artery and optic nerves. Originating from the dural endothelium, in many instances they grow both deeply and superficially, coming to involve the venous sinuses and overlying bone, be it the vertex or the base of the skull. Neighboring structures in many instances are of truly vital importance, and the surgeon is equally truly unwilling to sacrifice them to attain complete removal of the tumor. Additionally, there are some meningiomas which recur locally, even though apparently completely removed.

Here is an x-ray* and you will notice a big sort of a rock there. That is a meningioma, which is outlined by dye injected into the carotid artery. This is a typical hemispheral meningioma*. The

*Lantern slide photographs were used to illustrate the subject material. — Ed.

slide shows well the tumor attached to the overlying dura, which has been excised. You notice that there is superficial growth into the dura. The patient has now been well for approximately nine years.

It is difficult to speak definitely of the long-term prognosis in the majority of cases, although one may say generally that it is good. From time to time an occasional meningioma undergoes sarcomatous changes. Finally, the fact that the average age of operation in Harvey Cushing's series was 45 years suggests that intercurrent disease may antedate local recurrence, even when the removal has been incomplete.

Adenomas of the pituitary gland we hope will be treated in the future in the same way that thiouracil is used for hyperthyroidism. These patients, with the best available followups, after being successfully treated by surgery, have an incidence of symptomatic recurrence of 13 per cent over the first five years following operation. With close supervision, good long-term results may be anticipated in the majority of cases; but again, local recurrences after years, with extension into the brain, spot-light and perhaps unduly influence a surgeon's optimism about this type of patient.

Acoustic neuromas are among the most satisfying of intracranial tumors, for they are capable of total removal with a mortality rate which has been reduced steadily over the years, until now it should range between about 10 per cent or below. We have done about 150 in our center since Dr. McKenzie started. If we remove the tumor completely, a permanent cure results. These constitute only about 8 to 9 per cent of the tumors coming into a neurosurgical clinic.

Colloid cysts of the third ventricle, causing hydrocephalus, are equally permanent as to cure, if successfully removed, though no one neurosurgeon will perhaps come across more than a dozen in a busy lifetime.

*Psychosurgery* — Psychosurgery is a provoking and interesting subject. In 1935, Moniz in Portugal first interrupted the frontal association path in an attempt to relieve the pain and suffering of mentally ill patients. Since that time, thousands of patients have been operated upon all over the world. The experience with pre-

frontal lobotomy in this center has recently been described by Dr. A. Miller in a monograph based on the work of the Departments of Psychiatry and Neurosurgery in the University of Toronto, and published by the Department of Health in the Province of Ontario. Two features of this admirable monograph catch one's imagination.

First, of 144 chronically ill patients who had proven resistant to all forms of psychiatric therapy, 79 had improved sufficiently to leave the hospital. Of the 79 patients at home, 19 were working and living independent, socially-satisfactory lives. Sixteen were keeping house for their families, adjusting well, and entering into community social activities, while the remaining 44 at home required some supervision.

The second feature is that throughout the six-year period of study of these patients, a pre-operative assessment was made of what improvement might be anticipated from lobotomy, and follow-up of these patients to their homes and hospitals has been carried out to establish the accuracy of this pre-operative assessment. The result is that today a reasonable assurance is justified in arriving at a decision as to which patient will be benefited by prefrontal lobotomy.

I do not wish to go into psychosurgery further, save to emphasize to you that bilateral prefrontal lobotomy is not without cost to many patients in terms of their initiative, capacity to plan, and so on, and we in this Center regard it as the last resort.

*Cerebro-vascular Surgery* — Intracranial aneurisms* and arteriovenous malformations*, endangering the patient's life following rupture, constitute a hazard to life and cerebral function indefinitely. Aneurisms are tantalizing and provoking to surgeon and physician, for the lesion is curable if it can be eliminated surgically without interruption of an adequate supply of blood and oxygen to the brain. Various studies suggest that an estimate of .5 to one per cent indicates the incidence of intracranial aneurisms in the general population — asymptomatic for the most part.

Richardson and Hyland found 43 instances of intracranial

*Lantern slide photographs were used to illustrate the subject material. — Ed.

aneurism in 4,618 autopsies. Twenty-seven of these had ruptured, producing fatal hemorrhages. Seven were unruptured and had caused local pressure phenomena. An additional nine were incidental findings. The fluctuation in the reported incidence of aneurisms depends in part upon how careful is the search.

This patient* died of hydrocephalus, because this aneurism was of such a size that it was occluding the circulation of cerebral spinal fluid through the aqueduct of Sylvius. Here* is the picture of another brain. You see a large clot in the temporal lobe into which the aneurism had ruptured.

Here is another view* of this space-occupying lesion which suddenly developed, causing death.

That is the problem: How does one deal with a weak spot in the artery and the intracerebral hemorrhage? Again we are indebted to Moniz, who, in 1927, introduced cerebral angiography.

Here is an aneurism*. This patient had a subarachnoid hemorrhage, perhaps ten years before we did this cerebral angiogram. She went blind in the right eye ten years after her hemorrhage, and here is the cause, an aneurism pressing on the optic nerve. For a variety of personal reasons she could not contemplate surgical interference.

Following the introduction of angiography by Moniz, a few neurosurgeons on the continent of Europe began to undertake the surgical treatment of patients with subarachnoid hemorrhage due to rupture of an aneurism or arterio-venous malformation, and with encouraging results. However, it was not until after World War II that the problem of ruptured aneurisms was tackled extensively in North America.

Here is the angiogram* from a woman who was steadily deteriorating after having three subarachnoid hemorrhages in a matter of two weeks. You can follow the carotid artery up there. Here is half a dumbbell projecting forward, which is an aneurism. This patient was operated upon, and the aneurism trapped between two silver clips. Here is a re-check angiogram* and there is no aneurism, as you can see, two weeks later.

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*Lantern slide photographs were used to illustrate the subject material. — Ed.

The patients who have bled from a ruptured aneurism and have survived for eight weeks in a hospital are 50 per cent of the original group, and of the survivors an additional 25 to 35 per cent die in the years following discharge from the hospital, of vascular accidents. It is certain that the mortality rate in the first eight weeks of 50 per cent and the high incidence of recurrent hemorrhages following discharge from the hospital make a ruptured aneurism a grave problem.

At the present time, the neurosurgical literature contains many papers discussing the mortality rate occurring in patients who have been operated upon for an aneurism. Few of these publications differentiate sufficiently between cases dealt with in the first few days following a hemorrhage, and the patients who survive the high mortality of the first four weeks. Patients operated upon later represent quite a different and less difficult problem from those in the more acute phase.

In our personal series of 53 cases, we have 20 per cent mortality. I do not wish to emphasize these figures, because the series is not large enough, but we have operated upon many patients after their second hemorrhage, possibly during that two to three-week period which is perhaps unsuitable for operation.

From intensive study of this series as individual cases, it is clear to us that the late or quiet case can be dealt with with a very low mortality rate and a low incidence of disabling complications. This is, in fact, a form of prophylactic or preventative surgery aimed at preventing the recurrent hemorrhages which occur following discharge from the hospital in about 25 per cent of cases.

A problem more difficult of solution is the acute ruptured aneurism. In this group of patients, many centers have concluded the mortality rate and complications of surgical treatment are equally forbidding as the natural course of the disease. We are in the midst of a program of research, in an attempt to reduce the oxygen requirements of the brain during the period of surgical interference with an aneurism on the main vessel supplying important portions of the brain, for these aneurisms often rupture with even the most delicate manipulation.

My associate, Dr. William Lougheed, working at the Massa-

chusetts General Hospital Laboratories with Dr. William Sweet, carried out extensive experiments in animals, attempting to detour the blood around the aneurism, thus allowing safe and leisurely repair of the aneurism. He came finally to the use of general hypothermia which, as you know, has been established by Dr. William Bigelow as a valuable aid in cardiac surgery affording protection against anoxia.

Our preliminary observations on ten patients are encouraging, but it is much too soon to strike a balance against the protection we believe we obtain from anoxia on the one hand, and the risks of hypothermia in this type of case on the other hand.

We are greatly indebted to Dr. William Bigelow for his most valuable assistance and advice, and clearly we shall have to extend our electroencephalographic, electrocardiographic, temperature recording, and other observations during operation under hypothermia, in a number of directions.

Our experience, dating back now some six years, suggests that if the neck of the aneurism is firmly ligated or clamped, the patient is cured of that lesion.

Operations on aneurisms where patients have survived the initial period of hemorrhage shock, spasms of the blood vessels, and so on — that is, operations on aneurisms in the quiet stage, and having faced the 40 or 50 per cent mortality in the first six to eight weeks — have been achieved with a very low mortality in many places. Among the outstanding reports are those of Olivecrona in Stockholm and Poppen in Boston.

The other vascular lesion which should be of great interest to all of us is arterio-venous malformations, which have variously been called angiomas and varices. Hypotension — lowering of the blood pressure by chemical means — first made practical a local attack on aneurisms, and in like fashion has made even more practicable the excision of arterio-venous malformations of the brain which may cause death by intracerebral hemorrhage, as does an aneurism, by acting as a space-filling lesion with increased intracranial pressure, or by causing serial epileptiform seizures.

Here is such a lesion* exposed at operation. It is a most striking example of what has been called an angioma, and it is in fact an arterio-venous malformation with the arterial blood shunted through a fistula directly into the veins without the pressure toned down by the arterioles and capillaries, and one can see the blood flow through them at arterial speed. In this patient the diagnosis was made by angiography and excision of this whole mass has left the patient well.

Here is another interesting case*. This man, by contrast with the last one, had a fistula and you can see that cluster constituting an arterio-venous malformation, and just above it is a discoloration of the cortex. You can see that there is a ligature on this very large artery, and that was tied and the artery clipped. There was a large intracerebral clot. The next slide* shows the actual malformation, and this is a centimeter ruler, so it was very small. That was the cause of his trouble. The cure is so satisfactory that his wife, who had been sterile for some 20 years, promptly conceived following removal of the arterio-venous malformation.

There are many subjects I have not touched upon. E.g., we are interested in hemispherectomy in patients with infantile hemiplegia, temper tantrums and epilepsy.

I am afraid I have exceeded my time and I should now like to take the liberty of doing what I am not old enough to do. One is not supposed to "philosophize" or speculate concerning the future, I think, until shortly before one retires. However, the title of this paper is "Neurosurgery Today and Tomorrow" and I have given you an account of my personal experience and of our interest in neurosurgery today.

Every neurosurgeon held responsible for a university neurosurgical unit must of necessity try to peer into the future, for new units must be built, and if research is to be something more than a review of the activities of the past and an assessment of the doings of today, one must try to plan for the future. Advances in the management of cerebral tumors will rest upon the foundation of better understanding of the basic biological process involved

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*Lantern slide photographs were used to illustrate the subject material. — Ed.

in malignancy in the brain — and, indeed, everywhere. The psychosurgery of the future will be supported by the increasing understanding of the physiology of the brain and those structures which are gradually being defined as having a particular part to play in the physiology of emotion. The most extraordinary behavior problems and reactions and emotional disturbances can be reproduced from animal to animal by appropriate physiological changes. Local interference with these structures will be achieved by means of accurately placed needle electrodes, allowing local destruction of whatever area may be necessary with a minimum of mutilation of the brain.

It may be that ultra-sound, the placement of radioactive seeds emitting Beta radiation, or very sharply focused x-radiation, may be the agents of destruction. In like fashion, these technics may be applied to the amelioration of Parkinsonism and tremor. Advances in biochemistry and neurophysiology may well abolish the need for psychosurgery.

Finally, and of particular interest to insurance companies, will be the reduction of the mortality rate from subarachnoid hemorrhage due to ruptured aneurisms and ruptured arterio-venous malformations taken in the acute stage, for I believe permanent cure is possible, and that the number of these cases we and others have operated on bears no relation to their true incidence in the community.

"He who excuses himself accuses himself." That is an old proverb that my father used to quote to me in French, but it is with excuses that I have ventured upon these predictions of the future, because I shall be wrong, in all probability, on every one. Of one conviction I am certain: Whatever may be the future path of neurosurgery, the illustrious footsteps of our predecessors will be matched by the giant strides of our successors.

PRESIDENT MONTGOMERY — Thank you very much, Dr. Botterell. I am sure that somebody will have a question to ask.

QUESTION — Somebody reported on about 70 cases of pituitary adenoma treated by very high-voltage x-ray therapy. I would like to ask Dr. Botterell whether, in his opinion, x-ray therapy would

appear to be preferable to surgery, in so far as both immediate and late mortality is concerned.

DR. THEODORE M. EBERS — We will probably be getting some applicants for life insurance from this large group of patients who have had psychosurgery, and I suppose we will have to evaluate them largely on the psychiatric results. I would like to ask what extra hazards, if any, we must anticipate from the operative procedure itself.

DR. ALBERT J. ROBINSON — When we have completed the questions that will be asked of Dr. Botterell, I would like to suggest a rising vote of thanks to him, because I believe that this paper is going to be considered a masterpiece on the subject in our proceedings.

PRESIDENT MONTGOMERY — Thank you very much. Are there any other questions?

DR. BOTTERELL — It is really impossible for me to answer the first question about x-ray versus surgery of pituitary tumors, because some pituitary tumors are x-ray insensitive. There is no doubt that x-ray has been used with success without operation. I have heard the new very high-voltage work in Boston discussed, and we are also doing the same thing with cobalt 60 in Toronto. My own feeling is that it depends on how badly the optic nerves are damaged by pressure before the patient received treatment.

With eosinophilic adenomas, I think x-ray treatment by whatever modern method may be used has much to recommend it. It is subject to certain complications, as is surgery, but I think undoubtedly if a reactive edema and swelling can be safely accepted by the optic nerves, it has much to recommend it. However, I should not like to give any opinion on the question as to whether x-ray is better than surgery without qualifications.

Psychosurgery in this group of cases to which I have referred resulted in three deaths in 144 patients. As for the complications, there is the problem of post-traumatic epilepsy because of injury to the brain. The exact number of cases of epilepsy I cannot recall. I think it is of the order of 4 to 6 cases of epilepsy in 144 cases — none of which has proved unduly troublesome.

PRESIDENT MONTGOMERY — Thank you very much, Dr. Botterell.

Our last speaker for the meeting is Dr. Neil E. McKinnon, Professor of Epidemiology and Biometrics, School of Hygiene, University of Toronto.

It is always well to end any discussion with something good. We have therefore kept Dr. McKinnon until the last. Dr. McKinnon was born and brought up in the midst of other Scots in the village of Priceville, Grey County, Ontario, where he absorbed his first learning, graduating in Medicine from the University of Toronto in 1921. After spending some years as an intern in the Toronto General Hospital, he became attached to the Connaught Laboratory and School of Hygiene. Believing in the old saying that a rolling stone gathers no moss, he has stayed in that Institution ever since, taking time out from 1940 to 1944 to serve overseas in two Canadian Army Medical Corps hospitals as bacteriologist and pathologist. Dr. McKinnon has written many papers based on mortality figures, not only from the Province of Ontario, but for practically every other country from which such figures are available. He is especially interested in cancer mortality, and he is here this morning to tell us something about this subject.

# CANCER MORTALITY

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The fact that cancer stands in second place as a cause of death in our Western civilization is, by itself, of no great importance. As everyone knows, it is the age at which deaths occur that gives significance to their numbers. In the male, cancer accounts for 5 per cent of all the deaths in the age group of 20–29, 10 per cent in the 30–39 and for nearly 20 per cent by the age 60–69. In the female, cancer causes more than 10 per cent of the deaths in the age group 20–29, nearly 30 per cent in the 30–39 and 37 per cent of all deaths in the 40–49 age group. In both male and female, cancer mortality rates continue to increase as age advances, more so in the male than in the female, but other causes increase to a greater extent so as to far exceed cancer in older age. Over 60 per cent of all cancer mortality occurs before the age of three score years and ten. In the whole age group of 20–69, cancer accounts for nearly 17 per cent of all deaths in the male and over 27 per cent of all deaths in the female. Control of this untimely mortality would make a difference in insurance policy and practice.

How much control is possible? Over the past 25 to 30 years governments and the insurance groups and the public have contributed vast sums in an effort to control cancer mortality through early treatment. Breast cancer is the major cancer most accessible for early diagnosis and extensive treatment and the one held to be, therefore, the most susceptible to control. Examination of its recorded age-specific mortality in many areas reveals that (a) the rates, with the exception of those of the older age groups, maintain fairly level trends as their most constant and conspicuous feature; (b) although an occasional rate has fallen or otherwise diverged from the general pattern, the fall or other divergence is not consistent with the trends in other age groups in the same place, or is not maintained, or is not correlated in time and place

with control efforts and earlier treatment; (c) in general the rates of older age groups show a tendency, for varying periods, to increase. But it has been contended that the primary data, death certificates, are too lacking in accuracy[1,2,3] and the bookkeeping of them too unrealistic for the rates derived therefrom to serve as a reliable basis for comparison or for appraising the results of changes in treatment. In an investigation of the accuracy of recorded cancer mortality, Dr. Herbert L. Lombard, Director, Division of Cancer and other Chronic Diseases, Massachusetts Department of Public Health, examined hospital records and questioned the physicians supplying the death certificates in that State in 1932. By that means he found the recorded breast cancer mortality deficient by 10 per cent, some deaths actually due to breast cancer being classified in other categories. In 1939, the deficiency was 5 per cent and at the time of the report, 1952, it was less. Dr. Lombard attributes the improvement in the over-all deficiency from 10 per cent in 1932 to 5 per cent in 1939 and to less later to improvement in classification[1]. Such improvement in diagnosis, certification or bookkeeping is plainly reflected in the increase in the rates *in older age groups* in both Massachusetts and other places; that increase is of varying magnitude and duration. But, as far as the rates show and as far as general clinical and pathological experience would suggest, this change is practically confined to those age groups, the rates of other age groups, i.e. under older age, being little, if any, affected. Thus, with the over-all deficiency of the limited extent as noted, the deficiency in the rates for those under old age would certainly be very much less. If, on the other hand, the mortality charged to breast cancer under old age included, through inaccuracies in diagnosis, in certification or in bookkeeping, any material proportion of deaths due, in reality, to other causes, the rates would show either or both of two features — (a) a slight decline reflecting the real and marked decline in mortality from causes other than cancer in those age groups, (b) a change coincident with a change in selection of cause of death.* The fact that the rates do not in general exhibit

*The selection of the single cause of death from multiple causes was changed from the bookkeepers' responsibility, based on specified priorities, to the responsibility of the certifying physicians on the basis of their own opinion, in England and Wales about 1940, the United States of America 1948, and Canada 1950.

either of these features is good evidence, challenging contradiction, that they have not included any material proportion wrongly charged to breast cancer. (The diagnosis, certification or classification of cancer of other sites as breast cancer must be so very exceptional that it would not have any significant effect on the rates.) However, the precise degree of accuracy is bound to vary somewhat not only with age, but with time and place; and no one acquainted with the clinical, pathological or the statistical side of medicine should expect absolute accuracy for any age group for any place for any time.

But the persistence of practically level trends in breast cancer mortality under older age in each of the Canadian provinces despite vast differences between the control programs and changes in some of them, with the bookkeeping of all the provinces done by the Dominion Bureau of Statistics, and the similar persistence of similar level trends in that mortality in other areas (England and Wales, Massachusetts, New York, Minnesota, Missouri, Connecticut, Denmark), again despite vast differences between control programs and changes in some of them but with the bookkeeping under different auspices and, in some, a change during those years in selection of cause of death*, cannot be the result of chance or of possible influences, real or artificial, working in one direction, so regularly balancing and offsetting influences working in the opposite direction. This persistence of uniform level trends in rates derived from such diverse and changing circumstances leaves no reasonable doubt, (a) that although the recorded mortality from breast cancer in the past 25–30 years cannot be expected to be absolutely accurate, that in age groups under older age is sufficiently free from artifact to serve as a basis for appraising approximately the effects on mortality of general changes in treatment; (b) that the contention that reductions in mortality of breast cancer were offset by increases in its incidence requires the fantastic and therefore untenable assumption that such increases were practically proportional to reductions of varying magnitude, that contention is in itself untenable and must be rejected; (c) that there has been no material increase in the incidence of breast cancer in any

*See footnote on page 163.

area apart from that due to increase and ageing of the population; (d) that control programs providing earlier and more treatment have not achieved any decisive reduction in that mortality; and (e) as a necessary deduction, that in most, if not all, lethal breast cancer the remote metastases which are the eventual cause of death spread *from the primary lesion via the blood stream* before that spread can be interfered with — in other words, before the lesion can be detected and treated. That deduction, inescapable on critical consideration of all pertinent factors (the rates and their varying sources, the varying provision of diagnostic and therapeutic facilities, the varying degrees of increase and speeding up in treatment, the nature of the disease and its anatomical relationships [vertebral venous system[4]] and others) clashes with the premise on which control of breast cancer mortality was attempted. It implies that neither early nor extensive treatment of the primary lesion with its lymphatic drainage areas — almost from neck to pubis and within as well as without and across the chest wall — can materially reduce the mortality. And the lack, as far as is known, of any specific influence of the primary lesion on the *development* of metastases, after their implantation, excludes, albeit tentatively, the possibility of specifically *postponing* that mortality by treatment of the primary lesion and its regional foci.

Considerable emphasis has been laid on the development of cancer from "precancerous" states[5]. A possible inference is that the attack on cancer in the hope of reducing mortality should be carried further back to such conditions. As many of the programs that have failed in the control of cancer mortality included vigorous attack on all lumps and conditions considered possibly "precancerous", any such contention would appear to advocate what has already failed and of what leads to ever increasing treatment with further sacrifice of breast tissues but without material reduction of mortality. As Gatch and Culbertson[6] say of super-radical mastectomy, it would be "the triumph of hope over experience". The present inability to control mortality does not justify, for any age, what would be almost tantamount to mass mastectomy.

But deductions drawn from only one form of evidence can hardly be expected to carry complete conviction in the face of ingrained belief and data supporting it, especially when the source

of the confuting evidence is mortality statistics. Fortunately, those deductions do not have to stand alone. Critical studies in the pathological and clinical fields have reached quite similar conclusions. Sir James Paget[7] in London, in 1853 and Korteweg[8] in Amsterdam in 1880, were both convinced that early treatment was of little if any value in reducing mortality. But in recent years there has been a rapid succession, significant in itself, of analyses of cases showing consistently the limitations of early and extensive local and regional treatment. In mentioning some of those, it is worthy of note that Halsted[9] himself was conscious of the need for later appraisal of his radical mastectomy. Lewis and Rienhoff[10] (Hopkins) in 1932 indicated clearly the limitations of treatment — the surgeon could take no responsibility for the remote metastases which eventually would kill in "the large majority" of cases. Grace[11], New York, in 1937, concluded, "The cellular structure of the tumor is the dominant factor, and surgical technique, irrespective of the extent of its radicalism, plays a definitely secondary role." Handley and Thackray's[12] demonstration, 1947, that the majority (60 per cent) of breast cancers with axillary metastastes and about 10 per cent of those without axillary metastastes, show involvement of the internal mammary chain, findings fully confirmed by Wyatt[13], exposed *one* of the fallacies of "cleaning out" the axilla as practised for 50 years in the belief that the disease might be thereby eradicated. Truscott[14], The Middlesex Hospital, London, in 1947, puts his findings thusly: "This investigation has forced one to the conclusion that no matter how early the case or thorough the treatment, no patient is free from the possibility of recurrence until death occurs from some other cause." Bloom[15], of the same hospital, London, in 1950 said, "We are compelled to adopt the view that outcome in mammary cancer is determined largely by the histological type of growth, rather than by prompt treatment as soon as the lesion is discerned. MacDonald[16], Los Angeles, in 1951 wrote, ". . . to no small extent the doctrine of synonymy of 'early' treatment and curability should be recognized for the shibboleth which it is." Park and Lees[17], Edinburgh, in 1951 stated, "(a) It has not been proved that the survival rate of cancer of the breast, using the 5-year survival rate as an index, is affected by treatment at all. (b) The evidence strongly suggests that treatment is quite ineffectual in reducing the incidence of

death from metastatic spread. (c) If treatment is in any way effective, the effectiveness cannot be greater than that required to increase the over-all 5-year survival rate by more than 5 to 10 per cent." Haagensen and Stout[18], 1951, while still holding, apparently, to early treatment, present their findings with their customary and commendable frankness: "Although in our 1915–34 series of cases the cure rate fell with the increasing duration of the disease as would be expected, the data in the present series (1935–42) do not show such a correlation. We are unable to explain this finding." (This finding is, of course, not unique and, as will be noted later, the explanation of it would appear to be that the mortality pattern of any series is determined by the types of cases in that series and difference between the mortality patterns of two or more series is determined by difference in types of cases.) And their 281 ward patients with only 16.7 per cent of allegedly less than one month's duration and 35.6 per cent limited to breast had a 5-year survival rate of 51.6 per cent while their 214 private patients with 37.1 per cent of less than one month alleged duration and 42 per cent limited to breast had a 5-year survival rate of 44.9 per cent. (The authors properly point out that the results in the private cases are prejudiced by 17 cases being lost track of and computed as failures so that the difference between the results in public and private cases is not to be assumed to be of statistical significance.) Smithers et al[19], London, 1952 reported, "The most important factor in the prognosis in patients with breast cancer is the character of the tumors they develop." And in 1953, Williams, Murley and Curwen[20], in an analysis of 1044 cases treated at St. Bartholomew's Hospital (1930–1939), report: "The most impressive finding in this series, is the remarkable similarity in the survival rates following different methods of treatment. All the main treatment methods analyzed (simple mastectomy or excision of the lump, modified radical mastectomy, radical mastectomy, each with and without irradiation, and irradiation alone) seem to have been equally effective in stages 1 and 2. It must, however, be frankly recognized that all methods of treatment may have been equally ineffective in prolonging life . . . It might be expected that a method of treatment (radical mastectomy) which gives a low local recurrence index would also show a better over-all survival rate. It is, however,

possible that local recurrence *per se* is an infrequent source of distant metastases and that the appearance of the latter has been determined quite independently of the former." The uniformity in the 5-year survival rates in spite of drastic differences in treatment and thereby in local recurrences is further evidence that *the metastases that eventually cause death* spread early from the primary lesion and that later spread from secondary regional foci does not appreciably add to or hasten mortality. These and other findings from the clinical and pathological fields are thus in practically full conformity with the deductions drawn from the level trends in vital statistics.

What then of all the higher survival rates usually attributed to chronologically earlier treatment, or to treatment in an "early stage", or to more extensive or different treatment? Most of the reports of superiority of such differences in time or type of treatment are based, unfortunately, on comparisons of survival rates in series of cases the comparability of which could not be established or was, in retrospect, patently lacking. As an illustration of the fallacy of such comparisons, the difference between a 60 per cent over-all 5-year survival rate obtained in one series[21] and 43 per cent in another[22] can be cited to advantage. In both series practically all the cases were "proven" by microscopy. In the former series, however, 50 per cent of the cases were stage 1 while in the latter only about 16 per cent were so classified. Obviously this difference between proportions of stage 1 with its high survival rate (it will be noted later that stage is more an indication of type of tumor than of duration or developmental progress) would, in itself, explain, though not necessarily exclusively, the difference in the over-all survival rates. But the difference between 50 per cent and 16 per cent in the stage 1 proportions in the two series is as urgently in need of explanation. There is nothing to support the suggestion that it is due to the patients attending one clinic being more sensitive to signs and symptoms or more cancer-conscious, and thus presented themselves more promptly than those at the other. As the 5-year survival rate in the stage 1 cases in the former series (with 50 per cent stage 1) was not less, but slightly more, than in the stage 1 cases in the other series, the difference cannot be attributed to less adequate search for axillary

involvement in the former. As the clinic with 16 per cent of stage 1 cases did *not* have patients with a lesion first diagnosed as not cancer, returning later with obvious cancer in more than the very rare instance, if any, the difference cannot be attributed to this clinic missing early progressive cancer in the diagnosis. Thus, apparently the only reasonable explanation of the difference between the proportions classified as stage 1 is that it resulted from a difference in selection, i.e. diagnosis of cases, the clinic with the 50 per cent stage 1 diagnosing as cancer lesions which the other clinic diagnosed as not cancer. Thus, with such a wide difference in diagnosis between these two clinics of highest repute and difference thereby in type of cases and, consequently, in overall survival rates, it is obvious that neither uniformity in diagnosis, types of cases, nor in survival rates is to be expected in any two or more series of cases of different time or place, even though the diagnosis be "proven" by microscopy. On the contrary, difference of unknown and varying extent in diagnosis, and thereby in cases, and thus in survival rates is practically inevitable. And gross difference should be anticipated between two series of cases, one selected on the crucial criterion of death from breast cancer and the other on the basis that every lump is cancer until "proven" otherwise. Obviously deductions drawn from comparisons[22,23,24] of survival rates in such incomparable cases or even questionably comparable cases cannot carry weight, any difference in survival rates being reasonably attributable to difference in cases and, therefore, *not reliably* attributable to difference in time or type of treatment. Obviously, too, "proven" means only a miscroscopic picture indicative of cancer architecture but that picture does not indicate the biological nature, the metastatic or lethal propensity, on which the outcome depends. Only an estimate, not an invariably accurate appraisal, of that propensity can be made by the pathologist — an estimate or opinion exclusive of consideration of possible though still not definitely established host factors. Such an opinion is based solely on experience and training and on more intangible as well as more tangible factors (mitosis, differentiation, anaplasia) of not invariable significance. Thus reliable comparability cannot be assured even through microscopy.

But, it may be asked, does that not clash with what is known of the pathology of cancer? No, it does not. On the contrary,

it is the comparison of two or more series of cases without due regard for undetected or undetectable difference in types that clashes with what is known of the pathology of cancer. As early as 1923, Bloodgood[25] warned explicitly against the limitations of microscopy in differentiating between benign and malignant in borderline cases and, today, those limitations are generally recognized by pathologists[26]. The shortcomings of microscopy in diagnosing the biological character — the metastatic propensity — even of well developed breast tumors, were shown clearly by Lewis and Rienhoff in 1932. Lewison et al[27], 1953, after carefully reexamining the sections from patients who survived ten years or more reported, "These observations demonstrated that, at least in this series, the histological appearances alone could not have allowed one to prognosticate the 10-year survival that ensued." The shortcomings of microscopy have been observed in individual cases by all clinicians and pathologists of experience, and are reflected in the widespread efforts (staging, grading, grouping, combinations of these, animal and egg inoculations, tissue culture, and so on) of both clinicians and pathologists being made today in the hope (perhaps not well founded because the methods do not deal with host factors) of obtaining a sounder basis for prognosis than microscopy provides. What was considered almost rank heresy[28] when Greene[29] stated the case in 1945–1948 is now tacitly acknowledged in these efforts. Those previously censorious of his exposure of the limitations of histopathology now warn of the pitfalls in diagnosis and prognosis[30].

It is probably superfluous to mention again the fact recognized long ago[31] that the stage of a tumor bears little relationship to the duration. When alleged duration and stage are correlated, it is found that fully 50 per cent or more of the cancers of less than one month's duration have already involved the axilla. (Special examination by serial sections[32] or otherwise[6] would raise this figure considerably.) Park[33], 1949, found the increase in the proportion involving the axilla after onset of symptoms to be "so slight as to be hardly significant." Haagensen and Stout[18], 1951, found the increase to be from 56.5 per cent in 115 cases of less than one month's duration to 57.5 per cent in 174 cases of 1–5 month's duration and to only 68.8 per cent in 173 cases of six months or more. Stage 1 is still found in "cancers" of many

years duration[17]. Thus, with few exceptions, any "stage 1" must be suspected of progressing very slowly, *if at all,* to other stages, even if untreated. And any series of cases covering all durations in usual distribution but with stage 1 in a proportion as high as, e.g., 50 per cent has a proportion involving the axilla *over all durations* less than the proportion found involving the axilla in cancer of less than one month's duration — the whole is thus less than the part. Such high over-all proportions of stage 1, incompatible as they are with the stage 1 proportion found in metastasizing cancer of short duration, provide further evidence that "stage 1 cancers", if untreated, would not all progress to other stages but only a varying proportion might do so. Stage is thus more an indication of type of tumor than of duration or developmental progression. But even in this sense it has its limitations, remote metastases being found sometimes in the absence of regional metastases and sometimes not for many years, if at all, after the axilla is demonstrably and even massively involved. Survival rates in "stage 1 cancers" are not, therefore, indicative of survival rates in metastasizing cancers treated either chronologically early or in an early stage of development.

Other evidence purporting to show the superiority of early treatment is a decrease in 5-year survival rates with increasing pre-treatment durations — for a period — in patients selected and treated under the same auspices at the same time[23,34]. However, a decrease in 5-year survival rates has been actually observed, not merely assumed, in untreated fatal cases of increasing durations and therefore when found in treated cases cannot be confidently attributed to difference in time of treatment[35].

Thus, not only are the deductions drawn from the evidence in vital statistics well supported by critical evidence from other fields but none of the evidence supporting faith in superiority of early or different local and regional treatment is binding. Much of it patently fallacious and all of it is reasonably and consistently susceptible to other interpretations. It appears, therefore, to be a safe conclusion that breast cancer mortality is not susceptible to appreciable control through early or extensive treatment of the primary lesion and its lymphatic drainage areas.

Obviously when the control efforts have failed thus to reduce

mortality from breast cancer, evidence for the effectual control of mortality from cancer of any other major site should be required to be of unimpeachable character before it could be accepted.

The mortality records of other major cancers are far too inaccurate and too lacking in uniformity to provide any sound basis for the appraisal of early treatment. But the nearly level trends in the rates of all cancer (combined) in the female and of all cancer (combined) exclusive of pulmonary cancer in the male in the Ontario data, the inconsistency of declines in the rates for different age groups of all cancer (combined) in some places, and the apparent lack of correlation between those slight declines and control efforts leave no encouragement that effectual control of mortality from any major cancer has yet been achieved. No one, however, would place very much reliance on the data even of all cancer (combined) because they are too vulnerable to artificial influences. However, the higher survival rates reported for other major cancers are, as in breast cancer, readily explicable on the fallibility of comparisons of incomparable series — incomparable because of the present limitations of differentiation, microscopically, between metastasizing and non-metastasizing lesions and between those with a high and those with a low degree of metastatic propensity[26]. And, as in breast cancer, stage is more an indication of type than of duration or developmental progress. For instance, in a recent survey Dr. Crawford B. Shier[36] of Toronto, reported on 50 cases of "carcinoma-in-situ" in which the observation period varied from 1 to 14 years with an average of 4. Some of the cases showed similar lesions on repeated biopsy over many months, some were treated for other conditions, none was treated as for cancer, and 10 were not treated in any way but the lesion disappeared spontaneously, and none had progressed to invasive cancer. And Cannell[37] has recently reported from an analysis of cases that eradication of all accessible lymph-bearing tissue with vulval lesions does not give any assurance of eradication of the disease.

In conclusion, the past twenty-five to thirty years have given healed lesions in the breast in place of sloughing sores; have postponed death and given years of comfortable and useful life to many patients suffering from bowel and pelvic cancers which formerly killed for the most part by direct extension and related

complications; and they have given, more generally, gratifying cures of non-metastasizing cancers, such as most skin cancers or what are called cancers. They have provided a vast and varied experience which, from various fields, has demonstrated fallacy in our conceptions of the spread of cancer, fallacy and discrepancy, too, in diagnosis, and fallacy thereby in appraisal of the results of treatment. But in spite of earlier, more and more extensive treatment, they have not given any decisive reduction in mortality from metastasizing cancer.

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PRESIDENT MONTGOMERY — Now, there must be somebody who wants to ask a question about this subject.

DR. JOHN P. GEMMELL — I should like to ask Dr. McKinnon to draw some conclusions for me. From reading his articles, I have been able to end up in a dilemma: either that the treatment is of no value in breast carcinoma, or that simple mastectomy is of sufficient value.

Now, simple mastectomy has been used since approximately the turn of the century, so you would have to compare figures of 1940 to, perhaps, 1890; and the third alternative is that radical mastectomy is not radical mastectomy. So, as I say, I would like him to tell me whether he believes that treatment is of no value,

that simple mastectomy is adequate, or whether the thing is that there is no hope for further radical surgery.

DR. MCKINNON — Well, I am one of the old school. As I look on medicine its chief aim or function is to give relief, mental or physical.

I do not say anything against treatment. If treatment gives relief, mental or physical, medicine has achieved its highest objective. The only objection is to fooling ourselves.

Now, as far as simple mastectomy or radical mastectomy being the answer, well, I think your best answer to that, Dr. Gemmell, is in that beautiful series at St. Bart's—Reference 20. There they have over 1,000 cases all selected the same way and treated by the same people with different methods, and there the 5-year survival rates are identical, no matter what the treatment; but the local recurrence rates were very definitely higher with simple mastectomy than with radical mastectomy.

In other words, the greater local recurrence rate did not alter the 5-year survival rate. As far as I can see, that is the best evidence. Does that answer your question?

QUESTION — Dr. McKinnon, one frequently sees figures from various journals which, I think, do not have the difficulty of comparability that you spoke of. One sees figures with a radical mastectomy where the nodes are negative, and there is no recurrence for five, ten, fifteen, or twenty years. The expectation is appreciably greater than with simple mastectomy.

Now, I would like to be sure that I understood you. Is it your position that in the breast cancer where there is no metastasis, that these are not earlier ones, nor are the ones where there is metastasis into the nodes — that they are not necessarily later ones — but it is just a question of a difference in the type of the tumors themselves?

DR. MCKINNON — Yes. I have no thoughts, no opinions, except what the evidence shows. The evidence warrants one saying, however, without any question, that finding glands indicates a type, not duration; not time, but a type of tumor.

The absence of glands does not mean that it is not a spreading

cancer, but you can be assured that it is not likely to be. The evidence assures that.

Have I answered your question?

QUESTION — Yes, thank you.

PRESIDENT MONTGOMERY — Are there any other questions?

Thank you very much, Dr. McKinnon.

Gentlemen, we have now come to the conclusion of our scientific program. I want to thank all the guest speakers, on whom the success of any meeting depends. They provided us with an excellent program.

I wish to thank also those who took part in the discussion, because it is through their questions that things were sent moving along. Next I wish to thank Dr. Henry Kirkland, the Secretary of the organization. He has done a grand job and is a tower of strength, and I assure you that certainly in the last six weeks I have telephoned him every third day, and of course he had an answer right there.

To this I would also add that Miss Clara Rizzolo looks after details for us in the most competent manner.

I wish to thank the officers and members of all our committees, who have done such a fine job.

The time has now come for me to turn this meeting over to your new president, a fine gentleman who will guide our deliberations next year. I would just like to say that while the office of President entails some work, there is a great deal of pleasure also, and one realizes how many friends one has, people who are willing to help and do well every job that is given to them.

Any meeting depends also, in great part, I think, on the participation of the members. You have been a very good audience. Thank you very much!

I am now happy to turn over this meeting to your new president, Dr. Richard L. Willis, if he will come forward, please.

DR. RICHARD L. WILLIS — I wish to thank this organization for elevating me to this position, and I greatly appreciate the great honor. Somebody arranged to have this meeting include two

holidays. Next year's meeting will not be held on holidays. As most of you know, Monday, when some of us were here, was the Canadian Thanksgiving Day, and Tuesday was a holiday in many of our states — Columbus Day.

Now, one of our associates and I took a walk early Monday, and we were surprised that downtown Toronto here seemed to be almost completely deserted. We saw only a very few people and a rare car. It was not as deserted, however, as it was one Sunday last winter when there was a gentleman staying in this hotel who went out for a walk also, and he did not see anyone. He did not see a car.

Finally, however, he came to a policeman and he asked the policeman, "Where is everyone? The town is deserted."

The policeman said, "Well, the Catholics are all in church, the Protestants are all in bed, and the Jews are all in Florida."

Thanksgiving Day reminded me of a Manhattan family. They had a father, mother, and three children, and the father thought it would be a nice idea for each one to express gratitude for something that they were particularly thankful for. So he started off by saying that he was so thankful that he had such a happy family, and that they were all well and able to enjoy that wonderful day; and the mother named something that she was thankful for, and the oldest child, and the second child, and it came to little Johnnie who was five years old.

The father said, "Johnnie, what are you thankful for?"

He said, "Nothing."

"What do you mean? With all the things that you have, isn't there anything that you are thankful for?"

"Nothing."

"Well," the father said, "I think something must be done about this. You must have something that you are thankful for. What is it you want?"

He said, "I want a baby brother for Christmas."

Well, the father was an efficiency engineer. He said, "This is a big order, and this is pretty short notice."

And the youngster said, "I know. I've heard you say before when you got a big order on short notice that you put four or five good men on the job."

Next year's meeting will be held in New York at the Hotel Statler on October 19, 20 and 21. There will be some committee meetings on October 18th.

I wish to thank you again. And now, is there any further business?

DR. EARL C. BONNETT — Mr. President, it is my pleasure on behalf of our members to present this tribute of thanks and appreciation to those responsible for this inspiring 63rd annual meeting. It proposes a vote acknowledging our great indebtedness to the following:

1. Our outgoing President, Dr. Richard C. Montgomery, who has served this Association's interests loyally and faithfully during the year, and has concluded it with a challenging program of lasting interest.

2. The speakers who have opened new avenues to our future underwriting procedures by their splendid contributions to life insurance medicine. This includes the charming yet stirring address of Professor Long last night which dealt with underwriting in its broadest aspects.

3. The gracious hospitality of the officers of the Toronto insurance companies extended in the reception of Tuesday evening and also in the thoughtful program of entertainment for the ladies of our families.

4. The Australasian group which honored us with its presence and contributed to our scientific program. It is our earnest hope that we shall have them with us again in future meetings of the Association.

DR. WILLIS — I consider that a motion. Is there any second?

(The motion was seconded, was put to a vote, and was carried unanimously.)

The Secretary is authorized to cast a unanimous vote of thanks of this organization to Dr. Montgomery and his associates.

Is there any further business?

DR. W. J. MCCRISTAL — I am very glad that the grace of God has enabled me to enjoy the delights of this meeting. While I am on the subject I was wondering whether it might be suggested that it might be possible to hold one of these sessions in Australia. I do not think it is altogether outside the pale of possible realization in the future, and with the changes in our Australian money it may not be as cheap to buy, as time goes on, as you may think. So, it is probably later than you think, and beware of delaying such an objective. The time to be implementing it, perhaps, is now, or at least giving it some consideration.

I would like to thank the medical officers of the Association that it has been my privilege to visit, and the way they have opened their doors to me. And I thank you very much, sir, for giving me an opportunity to express my thanks for this privilege.

DR. WILLIS — We are glad to have Dr. McCristal's excellent suggestion. I am sorry that the arrangements have already been made, as I mentioned, for next year.

Is there any further business?

DR. VALENSULA — Mr. President, may I say a few words?

DR. WILLIS — Yes, sir.

DR. VALENSULA — Mr. President, it is a wonderful experience for me to have come here. I left my country on August 15 as one of five representatives of The Philippines. When I arrived in New York, I was invited by Dr. Cabot Lull, the Medical Director of the American Life Insurance Company to accompany

him to this convention. I thought that it was a wonderful opportunity to meet the medical directors of America, and so I gave him my consent.

I will go back to my country carrying with me this impression of wonderful hospitality, and I assure you that The Philippines will be most grateful for the very fine opportunity given to me by this whole convention. Thank you.

DR. WILLIS — Thank you very much. Is there any further business? If not, this meeting is adjourned.

# IN DEFENSE OF CIVILIZATION*

MARCUS LONG, M.A., Ph.D.
*Professor of Philosophy, University of Toronto*

Twenty-four hundred years ago Plato said you could measure the deterioration of a society by counting the number of doctors it employed. It is a mark of the progress of western civilization that today we reverse the judgment of Plato and measure the quality of a society by the medical services it provides. For the march of medicine has been one with the march of civilization.

It is true that science is the major influence shaping the culture of the western world and that engineering is the most effective way of translating scientific knowledge into more comfortable and adequate living. But the physical sciences and engineering have not contributed anything to compare with the easing of pain and the extension of life made possible by medical research. Science and Engineering build; they also frame the weapons of destruction. Medicine, when true to itself, seeks to bring only hope and healing. And let us remember that not even science has done more than medicine to rout the supporters of superstition, bigotry, ignorance and indifference who for so long tried to block the progress of man. Doctors are, without any question, largely responsible for the high quality of our modern civilization. It is proper, therefore, that I should talk to you doctors, not about medicine, but about the civilization you have helped to shape.

The first mark of our civilization is the place we give to women. The present status of women is one of the finest measures of our civilization. Doctors should be proud of the part they have played in their emancipation. There are no darker pages in history than those reporting the sufferings and dangers to which women used to be exposed in childbirth. It is a tragic reflection on man's knowledge of what is right and wrong that such brutalities should have been justified as part of the un-

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*Address delivered at the dinner of the Association of Life Insurance Medical Directors of America, Royal York Hotel, Toronto, on the evening of October 13, 1954.

changeable plan of God. Fortunately, there has been considerable improvement. Today we give our women the chance to live like human beings. And all of us are delighted. For like sensible men we agree with Martin Luther that "Who loves not women, wine and song, remains a fool his whole life long".

Another important phase of our civilization is the widespread interest in security.

The interest in security, and the need for it, is not something new. Poverty and hunger and social injustice have been the portion of man since the beginning of history. Some scholars find the source of modern religions in human despair, in the effort of man to find some meaning for his meaningless existence, in his search for consolation in his hours of tragedy.

The Hebrew prophets, who had no theory of immortality, dreamed of a time when God would intervene directly in history and rule the nations with justice for all. They dreamed of the time when nations would turn their swords into ploughshares, their spears into pruning hooks and make war no more. They dreamed of a golden age when no man would exploit his neighbor and every man enjoy his leisure in his own fruitful vineyard. It was a noble dream. But fundamentally it was no more than an effort to sustain the courage of those who were faltering before the cruelty of their fellows and the tragedies of life.

Christianity, like other religions, offered little hope for man in this world. Many Christian leaders taught their followers to submit to earthly circumstances, to accept without protest their station in life and its duties in the conviction that the wrongs of earth can only be corrected after death. While there are few clergymen today who accept this view, without qualification, a few years ago it was a widely held theory used to discourage serious attempts at reform.

Occasionally desperate men, not content to wait for justice after death, tried to solve their problems by force. The French Revolution was the most successful of such attempts. The success of this revolution established the belief that man can improve his lot in this life and that force is the best means of doing so. This theory found its classic expression in the philosophy of Karl

Marx. To counter this conception liberal philosophers agreed that man can improve his lot in this life but rejected revolution as a method because it is likely to breed greater evils than it destroys. They urged, as a better way, the use of the power of the state, as the servant of the people, to promote needed reforms for the good of all.

Today, in democratic countries this way of thinking, faced with the complications of modern society, has led to a reaffirmation of the power of the state. Modern men seem to believe that all troubles can be cured if only governments will take proper action. In North America the movement was sparked by the tragedy of the great depression and the need for the American government to intervene to prevent wholesale disaster. It has evolved into the concept of the social welfare state, now the accepted pattern in the United States and Canada. In the other main centre of democracy, the United Kingdom, the movement has taken, and continues to take, a form close to full socialism without quite getting there.

I am afraid of this movement although I cannot hide my sympathy for those who support it. Certainly it seems morally right that the prosperity of a country like Canada should be shared as fairly as possible among all the citizens. It seems morally wrong that any person should, through no fault of his own, suffer privation and poverty where there is more than enough for all. And certainly no one wants a repetition of the hungry thirties if intelligent and forceful action by the government can prevent it.

My main difficulty is that I fear a strong state more than I fear most of the other afflictions of life. Wherever the state gets too strong the rights of men are cancelled; their rights are treated as privileges which may be rescinded at any time. The state, treating itself as the source of law, refuses to be bound by the rule of law rooted in the moral insights and traditions of the people. There is, therefore, a danger that in the search for economic security we may forsake our history, that we may surrender our personal rights to rulers who may cancel them at their pleasure.

The pattern of tyranny is too well known for me to repeat its gory details. It is the danger of tyranny in our own development that is not so clearly seen. Our minds are so filled with the dangers outside we neglect the dangers within. They are just as real. What a tragedy if, in the twentieth century, we should, in the name of security, cancel the victories of our fathers and reestablish the power of the state they fought so bravely to limit.

That is our contemporary problem. I wish I could give you a sure answer to it. Unfortunately, I cannot. At best I can only make suggestions. The first is the paradox that the best protection against a too strong government is more government. This is not a new doctrine. It was written into both the American Constitution and the British North America Act as a division of powers. The difficulty is that today's circumstances call for a greater concentration of power in the hands of the central government than could have been foreseen. That makes the old doctrine of the division of powers difficult to maintain; it may even make the attempt to maintain it an obstacle to enlightened policy. That is the problem. I do not know where the line should be drawn. I only counsel that further power to the central government should be granted as grudgingly as possible.

In Canada the best way to keep the federal government from becoming too strong is to insist on the rights and powers of the provincial governments. Fortunately this is the doctrine accepted by both the liberal and conservative parties. It is denied by the CCF, the socialist party. The difficulty is that our defense effort and our social service program can only be carried out effectively by the central government. Hence some redistribution or reinterpretation of the powers of the several governments is required. Our problem is to give the central government the power it needs to perform its necessary functions without destroying the powers and privileges of the provinces. The United States has a similar problem. My suggestion is that in both countries we must be careful not to surrender too much of the authority of the provinces or states. Central government is a monster that fattens quickly; a monster that sooner or later will turn in its strength to destroy the individual.

My second suggestion is increased cooperation between big business and government for the general good. It is important to remember that one of the reasons for the increased power of government today was the failure of big business to control itself properly yesterday.

By this suggestion of greater cooperation between business and government you can see that I am stealthily approaching a problem that concerns yourselves, the demand for an extension of medical services to all the people under the direction of government. Let us be frank. The demand for some form of state medicine is increasing; it cannot much longer be denied. The liberal government in Canada has been stalling for twenty years on the plea that there is not enough hospital accommodation. Undoubtedly that is a fact, but I suspect it is not the reason. The problem of the Canadian government is to find a formula that will extend medical services to all the people without infringing on the rights of the provinces, increasing the burden of taxes beyond reason, or limiting the freedom of doctors.

Efforts have been made to find a solution, particularly through schemes offering hospital and medical services to those who are in a position to pay the premiums. The difficulty in these schemes, so far as I can understand them, is that they fail to protect the people who most need protection, the aged with limited means and the unemployed, because of their cost. As a result the medical expenses of these people too often fall on municipalities in no position to bear them. Why cannot our provincial governments, in cooperation with the insurance companies, develop a scheme that would provide protection for those who cannot afford protection, while leaving the others to look after themselves as at present? It seems to me quite feasible. Such cooperation would take care of those who need care without altering the basic pattern of our economy, increasing the power of government or infringing on the freedom of doctors.

Here I must offer apologies. An afterdinner speaker is supposed to be inspiring rather than instructive, entertaining rather than challenging. In any case I may have blundered badly in entering a field you people have no doubt canvassed more thoroughly than I. My only justification is that I am seriously

alarmed at the growing power of the state in our times, and I believe the establishment of state medicine would seriously increase it. An allpowerful state is a menace of the first order. If that threatened menace becomes a reality, it will only be because men have placed their selfish interests above the general good or refused to apply intelligence and compromise to social problems.

Our age is challenged to solve the problem of poverty, hunger and social insecurity. Modern science today makes a solution possible. There is no real justification for further delay; further delay is dangerous. Unless we can come up with a workable answer to the problem within our free institutions, impatient men will seek other solutions. I fear that these other solutions will involve the reestablishment of the allpowerful state, the end of freedom and responsible government.

A third characteristic of our civilization is the decline of interest in democracy. At the end of the 19th century, only 50 years ago, democracy was the triumphant political system. Herbert Spencer, the optimistic British philosopher, predicted that early in the 20th century democracy would be accepted by all civilized nations. He was tragically wrong.

By 1917 in Russia and 1922 in Italy the leaders of communism and fascism had seized power. They made no attempt to conceal their contempt for liberal democracy. Since then democracy has been in constant and increasing danger. Although fascism was emasculated on the battlefield, communism has flourished and grown in strength.

The progress of communism has been phenomenal. At the beginning of the 20th century communism was only a philosophy, an idea in the minds of a few men, many of whom were in prison. The workers of the world, apart from the IWW in the United States, were not enthusiastic about seizing the means of production from their employers by force.

In the summer of 1914 the leaders of the communist movement expected the workers to set their international interests as workers above their national loyalties as citizens in the war between Germany and her neighbors. They were bitterly disappointed

when the workers decided they were nationalists first and last and took arms to defend their respective countries. 1914 was a bleak year for the communist leaders. It is one of the great ironies of history that shortly after their great failure the communists should have been catapulted into power by the weakness of the Russian government and the scheming of the Germans.

From that rather shaky beginning which gave the communists control over a little more than 100 million people, they have advanced to control over more than 900 million people, more than ⅓ of the world's total population. During 1954 about 13 million more people were added to the total in Indo-China and there is every reason to expect that within the next few years millions more will go behind the iron curtain. With every seizure of territories and peoples the communists increase their stock of natural resources, their industrial capacity and their military strength. In 1954 we no longer confront a mere philosophy; we confront an armed power sufficiently strong to strike alarm in the hearts of all free men.

I have no time to discuss all the reasons for these events. It is obvious that one reason is the extension of the search for security I have already mentioned and the conviction that this security can, as Marx suggested, be attained only by force. The harsh, stark fact is that most of the people in the world are hungry. Only ⅓ of the world's people live in areas where sufficient food is available. ⅔ of the world's population goes to bed hungry every night.

It is unnecessary to point out to doctors that death from starvation is not the only consequence of hunger; there are also the diseases that flourish wherever there is malnutrition. The harsh, stark fact is that for this and other reasons in many sections of the world 50 per cent of all children die before the age of 5 and the general life expectancy floats around the age of 30.

It is in this wholesale human misery that communism flourishes for it offers to these people the promise of food and wellbeing in exchange for their freedom. An empty belly does not dwell on lofty principles; a hungry man will surrender his freedom for the promise of food. Wherever there are children dying who

need not die, wherever people are hungry who need not hunger, communism flourishes and will continue to flourish.

I do not wish to be an alarmist but it seems to me that democracy today is in deadly peril and may well perish within the next 50 years. It is well for us, then, to face up to the challenge and look to our defenses. Here again I am aware that I have nothing new to say and not even the time to treat adequately what I will say. But there are vital things which deserve to be repeated and repeated until there is no chance of our forgetting them.

The first answer is an elementary one; we cannot defeat communism by bullets. The 900 million people under communist rule cannot be rescued by military action initiated by us. Any politician or military leader who suggests either a preventive war or a war of liberation is suggesting a policy of folly. We are now in the atomic age; an age when war might well mean the elimination of the whole human race. The American government, it is reported, has developed a bomb so powerful two of them would wipe out the population of the Soviet Union. There is no reason to doubt that report. There is even less reason to doubt that the communists have weapons just as powerful.

That, if I may speak in parentheses for a moment, is one of the major dilemmas facing the framers of American foreign policy. Should an atomic war be started to defend southern Korea, the island of Quemoy or even the island of Formosa? Senator Knowland suggests it should. Mr. Dulles is silent. The communists are convinced that the American people would not countenance such a war for such a cause. They are, I believe, right. But that emphasizes our dilemma. Our reluctance to risk the elimination of all mankind gives the communists a chance to continue their policy of limited aggression against which we have no effective defense at present.

This does not mean we are left without weapons; we do have the weapons of food and industrial skill. With them we must make a concerted attack on hunger, seeking to remove the conditions which make communism so appealing to despairing men. The best protection I know against communism, apart from military strength, is a prosperous industrial community.

The major trouble in southeast Asia is the lack of industry and general prosperity. It is up to our governments to find an answer to that situation. It is not easy. There is a reluctance on the part of the less developed peoples to surrender their traditional ways of life for what they consider the materialism of the West, a fear on their part that any offer from the West may be a disguised attempt to continue the evils of colonialism, and the understandable reluctance of our own people to pay the cost.

Let us not deceive ourselves. Hunger cannot be eliminated and industry established in southeast Asia without money. Here the American government has set a worthy example for the rest of the free world. They have given generously and continue to give generously even if there are occasional rumblings of discontent from the taxpayers and some concessions to them. History will show, I believe, that the Marshall Plan and the Point Four Program were among the most generous and most inspired programs ever conceived and put into action by a government. It is necessary to continue what has been so well begun.

Our showing in Canada, although impressive in the light of our resources is still far short of what we can and should do. Our contributions are neither a measure of our prosperity nor of the great need.

The aid I am urging may not, in the long run, benefit us; those who take our gifts may turn to rend us. That is a risk we must take. The harsh stark fact is that unless we can solve the problem of human hunger or at least make an earnest attempt to solve it in the near future, we shall lose the chance, and perhaps the right, to survive.

But there is something else essential to our survival and that is a strong military organization; military power sufficient to protect us while we solve the economic problems. In the North Atlantic Treaty Organization we have a group of 14 nations contracted to pool their military strength in a common effort of defense. Fortunately because the atomic bomb was first developed by the United States these nations have been given time to build up sufficient military strength to discourage any military adventures by the Soviet Union. That is why western Europe has

been spared the horrors of communist invasion. NATO has been and continues to be a steel barrier protecting us from the barbarians.

However, NATO, as a military organization, depends on something more basic, the British-American alliance. So long as the British Commonwealth and the United States stand together there is no military power on earth that can beat us. All of us know that. Hence one might expect to find the peoples of Britain and the United States working fervently together, in the face of a common mortal danger, to make the alliance invincible. Unfortunately this is not so. We stress our disagreements rather than the many things we have in common and through bitter recrimination endanger our union. Men who ought to know better try to turn our differences into permanent divisions. By doing so they are either wittingly or unwittingly playing the communist game. Only the British-American alliance, as the centre of NATO, stands between communism and world conquest. Those who do or say anything threatening that alliance are strengthening the hands of the enemy. Unfortunately there are too many of them.

It is easy to point out the chief culprits but naming names is no solution to our problem. It merely intensifies our quarrels. How much better if we could ignore a Bevan and a McCarthy and give more attention to a Churchill and an Eisenhower. It is our good fortune that we have leaders around whom we may rally, leaders who stress our unity and seek to minimize our inevitable differences.

Let us be realistic as Sir Winston Churchill was last week. Without the United States the British Commonwealth would be subjugated and her beacon light of freedom snuffed out in the foul atmosphere of communist slavery. Without the British Commonwealth and the free nations of western Europe the United States could not defend herself successfully from this powerful and treacherous enemy.

Those British and American politicians who work for a split between Britain and the United States and try to drive the United States back into a lonely isolationism are playing a dangerous

game with our common safety. President Eisenhower and Mr. Stevenson are agreed on this. I wish that those in the United States and Britain who disagree would consider more carefully what they are doing. Our destiny is easy to read. We stand or fall on our united strength. There is no other way.

I must be careful. On these matters I feel so deeply it is easy to become too emotional. And yet I know you share my feelings; you must share my feelings. As doctors, associated for the most part with insurance companies, your primary interest is in your professional work. But you know, as well as I do, that the things you are trying to do can only be done in a world where freedom is secure. Destroy our free institutions and you destroy the possibility of your own work. What is even more important, you destroy the good society whose foundations were so bravely laid by our forefathers, you cancel out our free institutions and forge for all of us the shackles of slavery. That is why I have called on you to fight the tendency to create an all-powerful state in the name of security or, at least, support such measures as will limit the power of the state to destroy the souls and spirits of men. That is why I have called on you to support, by every means in your power, the only alliance, the Anglo-American alliance, that can frustrate the ambitions of our enemies.

In these dangerous days we cannot afford to strengthen our enemies by distrusting our friends. Let us differ where we must differ . . . that is the privilege of free men . . . but let us not, without real justification, seek to turn these differences into permanent divisions. The disagreements of free peoples can be resolved by friendly conferences and the use of intelligence. That is the genius of our way of life. There is no such easy escape from slavery. Spurn as you would the devil those men whose only stock in trade is slander against our allies. For such men, though they may pose as the friends of freedom, are its enemies.

I have spoken too long. Please accept my apology. Sometimes the heart runs away with the head. It is enough to point out that on all these matters I feel very deeply and speak very strongly because I am convinced that the way of freedom and only the way of freedom is the highway to man's noblest goals.

## MEMBERS PRESENT

The following doctors were present at some time during the sessions:

C. B. Ahlefeld
Joseph Altman
K. W. Anderson
J. A. Avrack

Bernard Baillargeon
N. J. Barker
J. R. Beard
J. E. Bee
M. B. Bender
C. C. Berwick
F. P. Bicknell
W. R. Bishop
W. C. Blackwell
J. E. Boland
William Bolt
E. C. Bonnett
C. M. Bonzey, Jr.
M. T. Boss
E. H. Botterell
K. F. Brandon
D. J. Breithaupt
H. J. Brekke
F. R. Brown
H. B. Brown
R. F. Buchan
C. A. Burroughs

N. S. Clark
M. H. Clifford
H. A. Cochran, Jr.
John Cole
N. B. Cole
G. R. Collyer
H. L. Colombo
F. R. Congdon
C. E. Cook
J. L. Cook
R. H. Craig

J. S. Delahaye
H. D. Delamere
F. R. Dieuaide
A. H. Domm
J. P. Donelan
T. C. Dunlop

T. M. Ebers
J. C. Emmett

J. G. Falconer
R. F. Farquharson
R. M. Filson
Clyde Fitts
P. M. L. Forsberg

D. S. Garner
J. H. Geddes
J. P. Gemmell
E. E. Getman
R. A. Goodell
George Goodkin
H. W. Goos
J. K. Gordon
C. D. Gossage
A. S. Graham
Ghent Graves
H. M. Gray
J. R. Gudger
V. W. Gunter

Llewellyn Hall
F. T. Hallam
J. H. Halliday
J. A. A. Harcourt
F. F. Harris
H. M. Hawkins
M. H. Henderson
R. E. Henning
John Hepburn
E. V. Higgins
A. A. Humphrey
J. H. Humphries
B. L. Huntington
J. R. B. Hutchinson

A. S. Irving
J. G. Irving

R. M. Janes
A. N. Jay
R. M. Johnson

E. A. Keenleyside
H. B. Kidd
N. C. Kiefer
D. G. Kilgore
Richard King
C. T. Kirchmaier
H. B. Kirkland
Edward Kuck
Paul Kurzweg, Jr.

E. R. Lamb
L. G. LaPointe
W. F. Larrabee, Jr.
H. R. Leffingwell
T. H. Lewis
E. H. Lindstrom
G. W. Lougheed
J. F. Lovejoy
G. J. Lunz

W. J. McCristal
William MacDonald
A. J. McGanity
F. J. McGurl
N. E. McKinnon
W. G. McLaughry
George McLean
L. L. McLellan
R. E. McLochlin
J. K. McShane
S. J. N. Magwood
R. W. Mann
F. A. L. Mathewson
L. K. Meredith
J. W. Merritt
L. C. Miller
M. B. Miller
E. S. Mills
Eugene Montgomery
R. C. Montgomery
C. V. Mulligan

R. M. Nay

A. J. Oberlander
W. F. H. O'Neill

A. E. Parks
J. S. Pearson
J. M. Peck
D. S. Pepper
Cullen Pitt
W. O. Purdy
R. S. A. Purkis

J. H. Ready
J. W. Reddick
C. L. Reeder
P. V. Reinartz
W. M. Reynolds
S. H. Richardson
D. F. Rikkers
R. C. Roadhouse
A. J. Robinson
R. C. Roskelley
W. W. Rucks
J. G. Ross

D. Y. Sage
J. L. Saia
H. C. Scadding
K. F. Schaefer
L. P. Schroeder
P. G. Schwager
B. T. D. Schwarz
W. H. Scoins

R. J. Scott
R. C. Secor
D. L. Selby
Hans Selye
E. F. Sheldon
J. T. Sheridan
R. R. Simmons
H. N. Simpson
J. C. Sinclair
B. W. Sitterson
Austin Smith
F. A. Snyder
W. H. Spittel
C. G. Spivey
P. D. Spohn
F. L. Springer
H. F. Starr
F. R. Stearns
E. M. Stevenson
L. O. Stewart
S. J. Streight
W. J. C. Symonds
J. C. Talbot
J. L. Tansey
M. J. Taylor
W. B. Thornton
H. M. Totman
Wallace Troup
F. D. Truax
H. E. Ungerleider
B. W. Vale
F. P. Valenzuela
R. C. Voss
P. C. Waldo
R. V. Ward
R. L. Weaver
S. S. Werth
J. A. Wilhelm
E. S. Williams
R. L. Willis
A. C. Wilson
C. L. Wilson
W. H. Wilson
J. S. Winder
C. H. Wirth
D. H. Woodhouse
L. S. Ylvisaker
D. E. Yochem
G. G. Young
V. H. Young
R. W. Zinkann

Also present were:

Professor Marcus Long
James Andrews, Jr.
Robert Beveridge
W. L. Fulghum
J. R. Gray
W. P. Marshall
L. N. Parker
John Ritchie
O. G. Sherman
George Skelding
W. M. Stufflebeem
J. C. Wilberding

Total attendance at all sessions, 215.

## In Memoriam

**Deceased since the Sixty-second Annual Meeting**

Henry H. Amsden, M. D.
United Life and Accident Insurance Company,
Concord, N. H.
Died September 14, 1954

Chester T. Brown, M. D.
The Prudential Insurance Company of America,
Newark, N. J.
Died November 11, 1953

Marvin L. Graves, M. D.
American General Life Insurance Company,
Houston, Tex.
Died November 19, 1953

John B. Nichols, M. D.
Acacia Mutual Life Insurance Company,
Washington, D. C.
Died February 22, 1954

James M. H. Rowland, M. D.
The Baltimore Life Insurance Company,
Baltimore, Md.
Died July 26, 1954

Marion Souchon, M. D.
Pan-American Life Insurance Company,
New Orleans, La.
Died April 2, 1954

Fred L. Wells, M. D.
Equitable Life Insurance Company of Iowa,
Des Moines 6, Iowa
Died September 17, 1953

George E. Woodford, M. D.
Home Life Insurance Company, New York City
Died May 24, 1954

## LIST OF MEMBERS OF THE ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA

| | |
|---|---|
| Fred B. Agee, Jr., M. D. | Aetna, Hartford, Conn. |
| Charles B. Ahlefeld, M. D. | Business Men's, Kansas City, Mo. |
| Henry Almond, M. D. | Metropolitan, New York City |
| Joseph Altman, M. D. | Companion Life, New York City |
| E. A. Anderson, M. D. | Modern Woodmen, Rock Island, Ill. |
| Frank R. Anderson, M. D. | Pacific Mutual, Los Angeles, Calif. |
| Karl W. Anderson, M. D. | Northwestern National, Minneapolis, Minn. |
| Perry A. Anderson, M. D. | Rockford Life, Rockford, Ill. |
| George B. Appleford, M. D. | Berkshire, Pittsfield, Mass. |
| Thomas M. Armstrong, M. D. | Philadelphia Life, Philadelphia, Pa. |
| William B. Aten, M. D. | Security Mutual, Binghamton, N. Y. |
| Donald R. Auten, M. D. | New York Life, New York City |
| J. Albert Avrack, M. D. | American Life, Wilmington, Del. |
| Bernard Baillargeon, M. D. | Alliance Nationale, Montreal, Canada |
| Norman J. Barker, M. D. | Connecticut General, Hartford, Conn. |
| Gordon P. Barnett, M. D. | Kansas City Life, Kansas City, Mo. |
| Charles M. Barrett, M. D. | Western and Southern, Cincinnati, Ohio |
| Samuel F. Bassett, M. D. | Prudential, Newark, N. J. |

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|---|---|
| Daniel S. Baughman, M. D. | Security Life and Accident, Denver, Colo. |
| Eliot F. Beach, Ph. D. | Metropolitan, New York City |
| J. Randolph Beard, M. D. | Mutual Benefit, Newark, N. J. |
| James E. Bee, M. D. | Kansas City Life, Kansas City, Mo. |
| Murray F. Bell, M. D. | New York Life, New York City |
| Maurice B. Bender, M. D. | Guardian, New York City |
| David M. Benford, M. D. | Metropolitan, New York City |
| Robert A. Benson, M. D. | Metropolitan, Ottawa, Canada |
| Roy W. Benton, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| C. Coleman Berwick, M. D. | Metropolitan, San Francisco, Calif. |
| Francis P. Bicknell, M. D. | State Mutual, Worcester, Mass. |
| B. Cosby Bird, M. D. | Preferred, Montgomery, Ala. |
| William R. Bishop, M. D. | Provident Life Acc., Chattanooga, Tenn. |
| F. Ray Black, M. D. | Great Southern, Houston, Tex. |
| Abraham Block, M. D. | Workmen's Benefit, Brooklyn, N. Y. |
| John E. Boland, M. D. | Country, Chicago, Ill. |
| William Bolt, M. D. | New York Life, New York City |
| John M. Bond, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Earl C. Bonnett, M. D. | Metropolitan, New York City |
| Charles M. Bonzey, Jr., M. D. | United States Life, New York City |
| M. Theodore Boss, M. D. | Home Friendly, Baltimore, Md. |
| John R. Bowen, M. D. | Penn Mutual, Philadelphia, Pa. |
| J. Thornley Bowman, M. D. | London Life, London, Canada |

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|---|---|
| Ernest L. Boylen, M. D. | Standard, Portland, Ore. |
| William R. Bradley, M. D. | Phoenix Mutual, Hartford, Conn. |
| William E. Branch, M. D. | Constitution Life, Los Angeles, Calif. |
| Kenneth F. Brandon, M. D. | Aetna, Hartford, Conn. |
| David J. Breithaupt, M. D. | Manufacturers, Toronto, Canada |
| Harvey J. Brekke, M. D. | Lutheran Brotherhood, Minneapolis, Minn. |
| Edmund J. Brogan, M. D. | Provident Mutual, Philadelphia, Pa. |
| Albert W. Bromer, M. D. | Metropolitan, New York City |
| C. Frank Brown, M. D. | Southwestern, Dallas, Tex. |
| Frederick R. Brown, M. D. | New England Mutual, Boston, Mass. |
| Howard B. Brown, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Ronald F. Buchan, M. D. | Prudential, Newark, N. J. |
| Carroll A. Burroughs, M. D. | Peoples, Frankfort, Ind. |
| Benjamin F. Byrd, M. D. | National Life & Accident, Nashville, Tenn. |
| Douglas B. Campbell, M. D. | National, Toronto, Can. |
| Edward J. Campbell, M. D. | New York Life, New York City |
| Hugh B. Campbell, M. D. | Phoenix Mutual, Hartford, Conn. |
| W. Allan Campbell, M. D. | Bankers, Lincoln, Neb. |
| Raymond L. Candage, M. D. | John Hancock Mutual, Boston, Mass. |
| David W. Carter, Jr., M. D. | Reserve Life, Dallas, Tex. |
| Paul H. Charlton, M. D. | Midland Mutual, Columbus, Ohio |
| Edmund D. Chesebro, M. D. | Puritan, Providence, R. I. |

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| Harry E. Christensen, M. D. | Union Mutual, Portland, Me. |
| Norman S. Clark, M. D. | Independent Order of Foresters, Toronto, Can. |
| Robert B. Cleveland, M. D. | Equitable Life Assurance, New York City |
| Milton H. Clifford, M. D. | New England Mutual, Boston, Mass. |
| Harry A. Cochran, Jr., M. D. | Lincoln National, Fort Wayne, Ind. |
| Norman B. Cole, M. D. | Baltimore Life, Baltimore, Md. |
| Irwin E. Colgin, M. D. | Texas Life, Waco, Tex. |
| G. R. Collyer, M. D. | London Life, London, Canada |
| Harry L. Colombo, M. D. | National Life, Montpelier, Vt. |
| Frederick R. Congdon, M. D. | Berkshire, Pittsfield, Mass. |
| Chester E. Cook, M. D. | Southwestern, Dallas, Tex. |
| J. Lindsay Cook, M. D. | Pilot, Greensboro, N. C. |
| Robert H. Craig, M. D. | Mutual, Waterloo, Can. |
| Neil L. Criss, M. D. | United Benefit, Omaha, Neb. |
| Howard K. Crutcher, M. D. | United Fidelity, Dallas, Tex. |
| Khurshed J. J. Cursetji, M. D. | Oriental Government Security Life, Bombay, India |
| Bryan A. Dawber, M. D. | Penn Mutual, Philadelphia, Pa. |
| John S. Delahaye, M. D. | Empire Life, Kingston, Canada |
| Harold D. Delamere, M. D. | Crown, Toronto, Canada |
| Aniceto Del Rio, M. D. | La Nacional, Mexico City, Mexico |
| Earle T. Dewey, M. D. | Metropolitan, San Francisco, Calif. |
| Edwin G. Dewis, M. D. | Prudential, Newark, N. J. |

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| Edward S. Dillon, M. D. | Penn Mutual, Philadelphia, Pa. |
| Harry W. Dingman, M. D. | Continental Assurance, Chicago, Ill. |
| Albert H. Domm, M. D. | Prudential, Los Angeles, Calif. |
| James P. Donelan, M. D. | Guarantee Mutual, Omaha, Neb. |
| Verner J. Donnelly, M. D. | Prudential, Houston, Tex. |
| Gerald D. Dorman, M. D. | New York Life, New York City |
| James T. Downs, Jr., M. D. | Fidelity Union, Dallas, Tex. |
| Raymond L. Dross, M. D. | Prudential, Houston, Tex. |
| Thomas C. Dunlop, M. D. | Manufacturers, Toronto, Canada |
| Louis B. Dunn, M. D. | Postal, New York City |
| William W. Eakin, M. D. | Standard, Montreal, Canada |
| Lyon H. Earle, Jr., M. D. | Connecticut General, Hartford, Conn. |
| Theodore M. Ebers, M. D. | Connecticut Mutual, Hartford, Conn. |
| H. Glenn Ebersole, M. D. | Central Standard, Monmouth, Ill. |
| Laurence B. Ellis, M. D. | Boston Mutual, Boston, Mass. |
| James C. Emmett, M. D. | Imperial, Toronto, Canada |
| Jack A. End, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Albert H. Faber, M. D. | New York Life, New York City |
| J. Gilbert Falconer, M. D. | North American, Toronto, Canada |
| Raymond K. Farnham, M. D. | Metropolitan, New York City |
| Haynes H. Fellows, M. D. | Metropolitan, New York City |
| William S. Fewell, M. D. | Liberty, Greenville, S. C. |

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| Ralph M. Filson, M. D. | Travelers, Hartford, Conn. |
| Rexford W. Finegan, M. D. | Metropolitan, New York City |
| Jack C. Fitzpatrick, M. D. | Prudential, Los Angeles, Calif. |
| Harry E. Flansburg, M. D. | Bankers, Lincoln, Neb. |
| James G. Forgerson, M. D. | Metropolitan, San Francisco, Calif. |
| Philip M. L. Forsberg, M. D. | United Life and Accident, Concord, N. H. |
| Garth E. Fort, M. D. | National Life & Accident, Nashville, Tenn. |
| John M. Foster, M. D. | Capitol, Denver, Colo. |
| John T. France, M. D. | State Farm, Bloomington, Ill. |
| Edward M. Freeland, M. D. | New York Life, New York City |
| Clarence E. Fronk, M. D. | Hawaiian Life, Honolulu, T. H. |
| Robert E. Funke, M. D. | Prudential, Los Angeles, Calif. |
| F. Irving Ganot, M. D. | Prudential, Newark, N. J. |
| I. Kenneth Gardner, M. D. | Lincoln National, Ft. Wayne, Ind. |
| David S. Garner, M. D. | Shenandoah, Roanoke, Va. |
| J. H. Geddes, M. D. | Northern, London, Canada |
| John T. Geiger, M. D. | Metropolitan, New York City |
| John P. Gemmell, M. D. | Monarch, Winnipeg, Canada |
| William M. Genthner, M. D. | Continental American, Wilmington, Del. |
| Edson E. Getman, M. D. | New York Life, New York City |
| Charles A. Gianasi, M. D. | Continental Assurance, Chicago, Ill. |
| Edgar G. Givhan, Jr., M. D. | Protective, Birmingham, Ala. |

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| Otto G. Goldkamp, M. D. | Connecticut General, Hartford, Conn. |
| Robert A. Goodell, M. D. | Phoenix Mutual, Hartford, Conn. |
| George Goodkin, M. D. | Equitable Life Assurance, New York City |
| Harold M. Goodman, M. D. | Home Beneficial, Richmond, Va. |
| Harry W. Goos, M. D. | Home, Philadelphia, Pa. |
| J. Keith Gordon, M. D. | Sun, Montreal, Canada |
| Charles D. Gossage, M. D. | Confederation, Toronto, Canada |
| Angus S. Graham, M. D. | London Life, London, Canada |
| George M. Graham, M. D. | Lincoln National, Fort Wayne, Ind. |
| Robert S. Graham, M. D. | Equitable Life Assurance, New York City |
| Albert E. Gras, M. D. | Prudential, Newark, N. J. |
| Ghent Graves, M. D. | American General, Houston, Tex. |
| Harris M. Gray, M. D. | Manufacturers, Toronto, Canada |
| Floyd M. Green, M. D. | Columbus Mutual, Columbus, Ohio |
| George E. Greenway, M. D. | Western Life Assurance, Hamilton, Canada |
| C. J. M. Grisdale, M. D. | Continental Assurance, Chicago, Ill. |
| Frederick O. Gronvold, M. D. | Pioneer Mutual, Fargo, N. D. |
| Richard S. Gubner, M. D. | Equitable Life Assurance, New York City |
| James R. Gudger, M. D. | Mutual, New York City |
| Van W. Gunter, M. D. | Jefferson Standard, Greensboro, N. C. |
| Milton W. Gwinner, M. D. | Western and Southern, Cincinnati, Ohio |

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| Llewellyn Hall, M. D. | Phoenix Mutual, Hartford, Conn. |
| F. Tulley Hallam, M. D. | Bankers, Des Moines, Iowa |
| John H. Halliday, M. D. | Australian Mutual, Sydney Australia |
| Gerald W. Halpenny, M. D. | Royal, Montreal, Canada |
| Vincent G. Hammond, M. D. | Security Mutual, Binghamton, N. Y. |
| Ottis E. Hanes, M. D. | Life Ins. Co. of Ga., Atlanta, Ga. |
| John A. A. Harcourt, M. D. | Toronto Mutual, Toronto, Canada |
| Frank F. Harris, M. D. | Volunteer State, Chattanooga, Tenn. |
| Garland M. Harwood, M. D. | Life Insurance Co. of Virginia, Richmond, Va. |
| Louis E. Hathaway, Jr., M. D. | Monarch, Springfield, Mass. |
| Howard L. Hauge, M. D. | New York Life, New York City |
| Walter C. Hausheer, M. D. | Prudential, Newark, N. J. |
| Harry M. Hawkins, M. D. | Old Line, Milwaukee, Wis. |
| Thomas L. Hawkins, M. D. | Western, Helena, Mont. |
| J. Harry Hayes, M. D. | Union, Little Rock, Ark. |
| Milton H. Henderson, M. D. | Excelsior, Toronto, Canada |
| Olin C. Hendrix, M. D. | New England Mutual, Boston, Mass. |
| William A. Henry, M. D. | Franklin, Springfield, Ill. |
| Ivan C. Heron, M. D. | West Coast, San Francisco, Calif. |
| William D. Hickerson, M. D. | Union Central, Cincinnati, Ohio |
| Eugene V. Higgins, M. D. | North American Reassurance, New York City |
| Ernest C. Hillman, Jr., M. D. | Mutual Benefit, Newark, N. J. |
| Daniel W. Hoare, M. D. | Penn Mutual, Philadelphia, Pa. |

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| Joseph C. Horan, M. D. | Metropolitan, New York City |
| Arnold B. Houston, M. D. | Great-West, Winnipeg, Canada |
| Edward G. Howe, M. D. | Prudential, Newark, N. J. |
| Thomas B. Hoxie, M. D. | New York Life, New York City |
| Henry W. Hudson, M. D. | Loyal Protective, Boston, Mass. |
| Gene I. Hull, M. D. | Bankers, Des Moines, Iowa |
| Merwin L. Hummel, M. D. | Acacia Mutual, Washington, D. C. |
| Arthur A. Humphrey, M. D. | Federal Life and Casualty, Battle Creek, Mich. |
| John L. Humphreys, M. D. | Lincoln National, Ft. Wayne, Ind. |
| James H. Humphries, M. D. | Home, New York City |
| J. Edward Hunsinger, M. D. | Republic Nat'l, Dallas, Tex. |
| Benjamin L. Huntington, M. D. | John Hancock Mutual, Boston, Mass. |
| Samuel W. Hurdle, M. D. | Security Life & Trust, Winston-Salem, N. C. |
| John J. Hutchinson, M. D. | New York Life, New York City |
| J. Raymond B. Hutchinson, M. D. | Acacia Mutual, Washington, D. C. |
| Albert S. Irving, M. D. | Commonwealth, Louisville, Ky. |
| J. Grant Irving, M. D. | Aetna, Hartford, Conn. |
| Tsugitake Isshiki, M. D. | Asahi Mutual, Tokyo, Japan |
| Samuel Jagoda, M. D. | State Reserve, Fort Worth, Tex. |
| Albert O. Jimenis, M. D. | Metropolitan, New York City |
| Hubert R. John, M. D. | Maccabees, Detroit, Mich. |

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| Joseph W. Johnson, Jr., M. D. | Interstate Life and Accident, Chattanooga, Tenn. |
| Alfred Kahn, Jr., M. D. | National Equity, Little Rock, Ark. |
| Victor L. Karren, M. D. | Home, New York City |
| Edward A. Keenleyside, M. D. | Prudential, Toronto, Canada |
| Frank J. Kefferstan, II, M. D. | John Hancock Mutual, Boston, Mass. |
| Charles H. Kelley, M. D. | Columbian National, Boston, Mass. |
| Newell R. Kelley, M. D. | Phoenix Mutual, Hartford, Conn. |
| Herbert B. Kennedy, M. D. | Woodmen of the World, Omaha, Neb. |
| William F. Ketchum, M. D. | New England Mutual, Boston, Mass. |
| Harry B. Kidd, M. D. | Metropolitan, Ottawa, Canada |
| Norvin C. Kiefer, M. D. | Equitable Life Assurance, New York City |
| Charles E. Kiessling, M. D. | Prudential, Newark, N. J. |
| Donald G. Kilgore, M. D. | Republic National, Dallas, Tex. |
| Richard King, M. D. | Family Fund, Atlanta, Ga. |
| Carl T. Kirchmaier, M. D. | Life & Casualty, Nashville, Tenn. |
| Henry B. Kirkland, M. D. | Prudential, Newark, N. J. |
| Norman L. Knott, M. D. | Prudential, Los Angeles, Calif. |
| Edward Kuck, M. D. | Union Central, Cincinnati, Ohio |
| Paul Kurzweg, Jr., M. D. | All American Assurance, Lafayette, La. |
| Ewart R. Lamb, M. D. | Paul Revere, Hamilton, Canada |
| Walter C. Lamb, M. D. | Equitable Life Assurance, New York City |
| Phillips Lambkin, M. D. | Guardian, New York City |

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| Paul H. Langner, Jr., M. D. | Provident Mutual, Philadelphia, Pa. |
| L. Gordon LaPointe, M. D. | Manhattan Life, New York City |
| H. Franklyn Laramore, M. D. | Connecticut Mutual, Hartford, Conn. |
| Walter F. Larrabee, Jr., M. D. | Minnesota Mutual, St. Paul, Minn. |
| Albert L. Larson, M. D. | Travelers, Hartford, Conn. |
| Ivan C. Lawler, M. D. | New York Life, New York City |
| Linford H. Lee, M. D. | Pacific Mutual, Los Angeles, Calif. |
| James M. Leffel, M. D. | Empire L. & A., Indianapolis Ind. |
| Harold R. Leffingwell, M. D. | Paul Revere, Worcester, Mass. |
| Charles P. LeRoyer, Jr., M. D. | Travelers, Hartford, Conn. |
| William R. Leute, Jr., M. D. | Penn Mutual, Philadelphia, Pa. |
| T. Herbert Lewis, M. D. | Western States, Fargo, N. D. |
| Janus C. Lindner, M. D. | Prudential, Minneapolis, Minn. |
| Everett H. Lindstrom, M. D. | Western, Helena, Mont. |
| James A. Livingston, M. D. | Liberty National, Birmingham, Ala. |
| Gladstone W. Lougheed, M. D. | Confederation, Toronto, Canada |
| John F. Lovejoy, M. D. | United Life, Jacksonville, Fla. |
| Cabot Lull, M. D. | American, Birmingham, Ala. |
| Gerald J. Lunz, M. D. | Knights of Columbus, New Haven, Conn. |
| Frank M. McChesney, M. D. | Equitable, Washington, D. C. |
| William J. McConnell, M. D. | Metropolitan, New York City |
| Howard M. McCue, Jr., M. D. | Life Insurance Co. of Virginia, Richmond, Va. |

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| Murdo G. MacDonald, M. D. | National, Montpelier, Vt. |
| William MacDonald, M. D. | Teachers Insurance & Annuity Association, New York City |
| Arthur J. McGanity, M. D. | Dominion, Waterloo, Canada |
| J. David McGaughey, III, M. D. | Connecticut General, Hartford, Conn. |
| Frank J. McGurl, M. D. | Prudential, Houston, Tex. |
| Thomas J. McGurl, Jr., M. D. | Mutual, New York City |
| Charles D. McKeown, M. D. | Farmers & Bankers, Wichita, Kan. |
| William G. McLaughry, M. D. | Protected Home Circle, Sharon, Pa. |
| George McLean, M. D. | Sun, Baltimore, Md. |
| Lawrence L. McLellan, M. D. | Provident Mutual, Philadelphia, Pa. |
| Ralph E. McLochlin, M. D. | National Old Line, Little Rock, Ark. |
| William J. McNamara, M. D. | Equitable Life Assurance, New York City |
| Charles D. Magee, M. D. | Missouri Insurance Company, St. Louis, Mo. |
| Morton Magiday, M. D. | Equitable Life Assurance, New York City |
| S. J. Newton Magwood, M. D. | Continental, Toronto, Canada |
| John Malgieri, M. D. | New York Life, New York City |
| Peter V. Martin, M. D. | Prudential, Minneapolis, Minn. |
| Francis A. L. Mathewson, M. D. | Great-West, Winnipeg, Canada |
| Loren K. Meredith, M. D. | National, Des Moines, Iowa |
| John W. Merritt, M. D. | Dominion, Waterloo, Canada |
| Ignacio Mesa, M. D. | "La Latino-Americana", Mexico City, Mexico |
| Lloyd C. Miller, M. D. | National Life & Accident, Nashville, Tenn. |

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| Milton B. Miller, M. D. | Victory Life, Topeka, Kan. |
| Edward S. Mills, M. D. | Prudential Assurance, Montreal, Canada |
| Eugene Montgomery, M. D. | North American, Toronto, Canada |
| Richard C. Montgomery, M. D. | Manufacturers, Toronto, Canada |
| John F. Moore, Jr., M. D. | Mutual, New York City |
| Samuel R. Moore, M. D. | Provident Mutual, Philadelphia, Pa. |
| J. R. E. Morden, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Reuben A. Moser, M. D. | American Reserve, Omaha Neb. |
| J. Palmer Moss, M. D. | Columbian Mutual, Memphis, Tenn. |
| Bernard Mount, M. D. | All States, Montgomery, Ala. |
| Elmer B. Mountain, M. D. | American Mutual, Des Moines, Iowa |
| Clifford V. Mulligan, M. D. | T. Eaton, Toronto, Canada |
| Frederick D. Munroe, M. D. | Fidelity, Regina, Canada |
| Luiz Murgel, M. D. | Companhia Internacional, Rio de Janeiro, Brazil |
| George H. Murphy, M. D. | Maritime, Halifax, Canada |
| Sidney A. Narins, M. D. | Mutual, New York City |
| Richard M. Nay, M. D. | Indianapolis Life, Indianapolis, Ind. |
| Mather H. Neill, M. D. | Aetna, Hartford, Conn. |
| Clive P. Neilson, M. D. | Sovereign Life, Winnipeg, Canada |
| Richard A. Nelson, M. D. | Prudential, Jacksonville, Fla. |
| Richard E. Nicholson, M. D. | Connecticut Mutual, Hartford, Conn. |

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| Andrew J. Oberlander, M. D. | Prudential, Chicago, Ill. |
| William L. O'Connell, M. D. | Union Labor, New York City |
| Robert D. O'Connor, M. D. | Old Line, Milwaukee, Wis. |
| Robert J. Oehrig, M. D. | Home, New York City |
| Denis J. O'Leary, M. D. | New York Life, New York City |
| Martin I. Olsen, M. D. | Central, Des Moines, Iowa |
| William F. H. O'Neill, M. D. | Franklin, Springfield, Ill. |
| John K. T. Ormrod, M. D. | Aetna, Hartford, Conn. |
| Wilbert C. Page, M. D. | Prudential, Newark, N. J. |
| Arthur E. Parks, M. D. | Canada Life, Toronto, Canada |
| John S. Pearson, M. D. | American United, Indianapolis, Ind. |
| John McC. Peck, M. D. | John Hancock Mutual, Boston, Mass. |
| D. Sergeant Pepper, M. D. | Connecticut Mutual, Hartford, Conn. |
| Gilberto S. Pesquera, M. D. | Metropolitan, New York City |
| Charles A. Peters, M. D. | Prudential Assurance, Montreal, Canada |
| Ray W. Peterson, M. D. | Columbian Mutual, Binghamton, N. Y. |
| Cullen Pitt, M. D. | Atlantic, Richmond, Va. |
| Theodore E. Plucinski, M. D. | Mutual, New York City |
| Albert A. Pollack, M. D. | Mutual, New York City |
| Roscoe W. Pratt, M. D. | New York Life, New York City |
| William O. Purdy, M. D. | Equitable, Des Moines, Iowa |
| Raymond S. A. Purkis, M. D. | Canada Life, Toronto, Canada |
| Michael A. Puzak, M. D. | Peoples, Washington, D. C. |
| Louis A. Pyle, M. D. | Colonial, East Orange, N. J. |

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| O. Samuel Randall, M. D. | Midland National, Watertown, S. D. |
| Paul M. Rattan, M. D. | Great National, Dallas, Tex. |
| James H. Ready, M. D. | General American, St. Louis, Mo. |
| Rezin Reagan, M. D. | National Reserve, Sioux Falls, S. D. |
| Clifton L. Reeder, M. D. | Continental Assurance, Chicago, Ill. |
| Paul V. Reinartz, M. D. | Prudential, Jacksonville, Fla. |
| Whitman M. Reynolds, M. D. | Equitable Life Assurance, New York City |
| H. Guy Riche, M. D. | Guaranty Income, Baton Rouge, La. |
| Donald F. Rikkers, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Robert C. Roadhouse, M. D. | Prudential, Toronto, Canada |
| George P. Robb, M. D. | Metropolitan, New York City |
| David C. Roberts, M. D. | Guardian, New York City |
| Albert J. Robinson, M. D. | Connecticut General, Hartford, Conn. |
| John C. Robinson, M. D. | Travelers, Hartford, Conn. |
| Van C. Robinson, M. D. | American Mutual, Des Moines, Iowa |
| Henry B. Rollins, M. D. | Connecticut Mutual, Hartford, Conn. |
| Gordon Ross, M. D. | Massachusetts Mutual, Springfield, Mass. |
| John G. Ross, M. D. | Mutual, Waterloo, Canada |
| Thomas F. Ross, M. D. | Ohio State, Columbus, Ohio |
| John A. Rossa, M. D. | Equitable Life Assurance, New York City |
| Edward W. Rowe, M. D. | Midwest, Lincoln, Neb. |
| William W. Rucks, M. D. | Home State, Oklahoma City, Okla. |
| John K. Ruggles, Jr., M. D. | Paul Revere, Worcester, Mass. |
| Merlin T. Ryman, M. D. | Mutual Benefit, Newark, N. J. |

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|---|---|
| Dan Y. Sage, M. D. | Southern, Atlanta, Ga. |
| John L. Saia, M. D. | National, Montpelier, Vt. |
| Joe H. Sanderlin, M. D. | First Pyramid Life, Little Rock, Ark. |
| Raymond C. Scannell, M. D. | Security Life and Accident, Denver, Colo. |
| Royal S. Schaaf, M. D. | Prudential, Newark, N. J. |
| Kenneth F. Schaefer, M. D. | Prudential, Minneapolis, Minn. |
| Robert B. Schlesinger, M. D. | Mutual Trust, Chicago, Ill. |
| Louis Schwab, M. D. | Union Central, Cincinnati, Ohio |
| Paul G. Schwager, M. D. | Equitable, Waterloo, Canada |
| Berthold T. D. Schwarz, M. D. | Bankers National, Montclair, N. J. |
| William H. Scoins, M. D. | Lincoln National, Ft. Wayne, Ind. |
| Robert J. Scott, M. D. | Michigan Life, Detroit, Mich. |
| Ralph C. Secor, M. D. | Liberty National, Birmingham, Ala. |
| Alfred F. Seibert, M. D. | Travelers, Hartford, Conn. |
| David L. Selby, M. D. | Imperial, Toronto, Canada |
| Thomas S. Sexton, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Hall Shannon, M. D. | Southland, Dallas, Tex. |
| Elroy F. Sheldon, M. D. | Occidental, Los Angeles, Calif. |
| Joyce T. Sheridan, M. D. | Fidelity Mutual, Philadephia, Pa. |
| Hubert H. Shook, M. D. | Ohio National, Cincinnati, Ohio |
| Ralph R. Simmons, M. D. | Equitable, Des Moines, Iowa |
| Howard N. Simpson, M. D. | Monarch Life, Springfield, Mass. |
| Richard B. Singer, M. D. | New England Mutual, Boston, Mass. |

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| Beecher W. Sitterson, M. D. | Ohio National, Cincinnati, Ohio |
| James R. Slamer, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| F. Hartley Smith, M. D. | Great-West, Winnipeg, Canada |
| Stewart A. Smith, M. D. | Australian Mutual, Sydney, Australia |
| Wilbur A. Smith, M. D. | Equitable Life Assurance, New York City |
| Frederick A. Snyder, M. D. | Western and Southern, Cincinnati, Ohio |
| Isaac Sossnitz, M. D. | Eastern, New York City |
| Wallace H. Spittel, M. D. | Canada Life, Toronto, Canada |
| Charles G. Spivey, M. D. | Carolina Life, Columbia, S. C. |
| Frank L. Springer, M. D. | Columbian National, Boston, Mass. |
| H. Frank Starr, M. D. | Jefferson Standard, Greensboro, N. C. |
| F. R. Stearns, M. D. | Security Benefit, Topeka, Kan. |
| George G. Stebbins, M. D. | Wisconsin Life, Madison, Wis. |
| David F. R. Steuart, M. D. | Mutual Benefit, Newark, N. J. |
| Edgar M. Stevenson, M. D. | State Farm, Bloomington, Ill. |
| Hector M. Stevenson, M. D. | Aetna, Hartford, Conn. |
| Lester Q. Stewart, M. D. | Aetna, Hartford, Conn. |
| Frank M. Stites, M. D. | Kentucky Home Mutual, Louisville, Ky. |
| John C. Talbot, M. D. | Pacific Mutual, Los Angeles, Calif. |
| Joseph L. Tansey, M. D. | John Hancock Mutual, Boston, Mass. |
| Louis J. Tedesco, M. D. | New York Life, New York City |
| Gamber F. Tegtmeyer, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Edward R. Thompson, M. D. | Texas Prudential, Galveston, Tex. |

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| K. Jefferson Thomson, M. D. | Metropolitan, New York City |
| William B. Thornton, M. D. | Norwich Union, Toronto, Canada |
| Joel E. Toothaker, M. D. | Sunset Life, Olympia, Wash. |
| Albert R. Tormey, M. D. | National Guardian, Madison, Wis. |
| Grafton D. Townshend, M. D. | Standard Life Association, Lawrence, Kan. |
| Joseph Travenick, Jr., M. D. | Occidental, Los Angeles, Calif. |
| Wallace Troup, M. D. | Metropolitan, Ottawa, Canada |
| Francis D. Truax, M. D. | Crown, Toronto, Canada |
| Maurice Turcotte, M. D. | Industrial, Quebec, Canada |
| Harry E. Ungerleider, M. D. | Equitable Life Assurance, New York City |
| Bruce W. Vale, M. D. | Excelsior, Toronto, Canada |
| Alexander E. Venables, M. D. | Minnesota Mutual, St. Paul, Minn. |
| Frederick H. Vinup, M. D. | Monumental, Baltimore, Md. |
| Reynold C. Voss, M. D. | Pan-American, New Orleans, La. |
| Proctor C. Waldo, M. D. | Washington National, Evanston, Ill. |
| B. Lincoln Wales, Jr., M. D. | Massachusetts Mutual, Springfield, Mass. |
| George H. Walker, M. D. | Lincoln Liberty, Lincoln, Neb. |
| Dick P. Wall, M. D. | American National, Galveston, Tex. |
| Gordon K. Wallace, M. D. | Great American Reserve, Dallas, Tex. |
| Kenneth E. Ward, M. D. | Connecticut General, Hartford, Conn. |

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| R. Vance Ward, M. D. | Montreal Life, Montreal, Canada |
| Frank A. Warner, M. D. | John Hancock Mutual, Boston, Mass. |
| Robert L. Weaver, M. D. | Penn Mutual, Philadelphia, Pa. |
| Jefferson Weed, M. D. | Mutual Benefit, Newark, N. J. |
| John A. Wilhelm, M. D. | Gulf, Jacksonville, Fla. |
| Alfred A. Willander, M. D. | Mutual Trust, Chicago, Ill. |
| Earl B. Williams, M. D. | Wisconsin National, Oshkosh, Wis. |
| Ennion S. Williams, M. D. | Life Insurance Co. of Virginia, Richmond, Va. |
| Richard L. Willis, M. D. | Mutual, New York City |
| Archibald C. Wilson, M. D. | Connecticut General, Hartford, Conn. |
| C. L. Wilson, M. D. | Empire State Mutual, Jamestown, N. Y. |
| John S. Winder, M. D. | London Life, London, Canada |
| Don J. Wolfram, M. D. | Jefferson National, Indianapolis, Ind. |
| Donald H. Woodhouse, M. D. | Sun, Montreal, Canada |
| Lauritz S. Ylvisaker, M. D. | Fidelity Mutual, Philadelphia, Pa. |
| Donald E. Yochem, M. D. | Farm Bureau, Columbus, Ohio |
| Arthur W. Young, M. D. | Sun, Montreal, Canada |
| George G. Young, M. D. | Central, Des Moines, Iowa |
| Victor H. Young, M. D. | Travelers, Hartford, Conn. |
| Russell W. Zinkann, M. D. | Mutual, Waterloo, Canada |
| Arthur R. Zintek, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Albert F. Zipf, M. D. | Calif.-Western States, Sacramento, Calif. |

## HONORARY MEMBERS

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| Francis R. Dieuaide, M. D. | New York City |
| Arthur Hunter | New York City |
| Edward E. Rhodes | Newark, N. J. |

## EMERITUS MEMBERS

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| John W. Abbott, M. D. | Worcester, Mass. |
| Edwin H. Allen, M. D. | Boston, Mass. |
| Hiram H. Amiral, M. D. | Worcester, Mass. |
| William B. Bartlett, M. D. | Boston, Mass. |
| Edgar W. Beckwith, M. D. | New York City |
| O. M. Eakins, M. D. | Pittsburgh, Pa. |
| Harold M. Frost, M. D. | Boston, Mass. |
| Frank Harnden, M. D. | Pittsfield, Mass. |
| Byam Hollings, M. D. | Boston, Mass. |
| Walter A. Jaquith, M. D. | Columbus, Ohio |
| Albert E. Johann, M. D. | Des Moines, Iowa |
| George McCreight, M. D. | Des Moines, Iowa |
| Francis H. McCrudden, M. D. | Boston, Mass. |
| William Muhlberg, M. D. | Cincinnati, Ohio |
| Herbert Old, M. D. | Philadelphia, Pa. |
| George P. Paul, M. D. | Hartford, Conn. |
| Charles B. Piper, M. D. | Hartford, Conn. |
| Walter A. Reiter, M. D. | Newark, N. J. |
| Robert L. Rowley, M. D. | Hartford, Conn. |
| H. Crawford Scadding, M. D. | Toronto, Canada |
| Ernest W. Scott, M. D. | New York City |
| John B. Steele, M. D. | Chattanooga, Tenn. |
| Samuel J. Streight, M. D. | Toronto, Canada |
| Bion C. Syverson, M. D. | New York City |
| Walter E. Thornton, M. D. | Fort Wayne, Ind. |
| William R. Ward, M. D. | Newark, N. J. |
| Chester F. S. Whitney, M. D. | New York City |
| McLeod C. Wilson, M. D. | Hartford, Conn. |

## COMPANIES AND THEIR REPRESENTATIVES

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| Acacia Mutual Life Insurance Co., Washington, D. C. | M. L. Hummel, M. D.<br>J. R. B. Hutchinson, M. D. |
| Aetna Life Insurance Co., Hartford, Conn. | F. B. Agee, Jr., M. D.<br>K. F. Brandon, M. D.<br>J. G. Irving, M. D.<br>M. H. Neill, M. D.<br>J. K. T. Ormrod, M. D.<br>H. M. Stevenson, M. D.<br>L. Q. Stewart, M. D. |
| Alliance Nationale, Montreal, Canada | Bernard Baillargeon, M. D. |
| All American Assurance Co., Lafayette, La. | Paul Kurzweg, Jr., M. D. |
| All States Life Insurance Co., Montgomery, Ala. | Bernard Mount, M. D. |
| American General Life Insurance Co., Houston, Tex. | Ghent Graves, M. D. |
| American Life Insurance Co., Birmingham, Ala. | Cabot Lull, M. D. |
| American Life Insurance Co., Wilmington, Del. | J. A. Avrack, M. D. |
| American Mutual Life Insurance Co., Des Moines, Iowa. | E. B. Mountain, M. D<br>V. C. Robinson, M. D. |
| American National Insurance Co., Galveston, Tex. | D. P. Wall, M. D. |
| American Reserve Life Insurance Co., Omaha, Neb. | R. A. Moser, M. D. |
| Asahi Mutual Life Insurance Company, Tokyo, Japan | Tsugitake Isshiki, M. D. |

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| American United Life Insurance Co., Indianapolis, Ind. | J. S. Pearson, M. D. |
| Atlantic Life Insurance Co., Richmond, Va. | Cullen Pitt, M. D. |
| Australian Mutual Provident Society, Sydney, Australia. | J. H. Halliday, M. D.<br>S. A. Smith, M. D. |
| Baltimore Life Insurance Co., Baltimore, Md. | N. B. Cole, M. D |
| Bankers Life Company, Des Moines, Iowa. | F. T. Hallam, M. D.<br>G. I. Hull, M. D. |
| Bankers Life Insurance Co. of Nebraska, Lincoln, Neb. | D. A. Campbell, M. D.<br>H. E. Flansburg, M. D. |
| Bankers National Life Ins. Co., Montclair, N. J. | B. T. D. Schwarz, M. D. |
| Berkshire Life Insurance Co., Pittsfield, Mass. | G. B. Appleford, M. D.<br>F. R. Congdon, M. D. |
| Boston Mutual Life Insurance Co., Boston, Mass. | L. B. Ellis, M. D. |
| Business Men's Assurance Co. of America, Kansas City, Mo. | C. B. Ahlefeld, M. D. |
| Calif.-Western States Life Insurance Co., Sacramento, Calif. | A. F. Zipf, M. D. |
| Canada Life Assurance Co., Toronto, Canada. | A. E. Parks, M. D.<br>R. S. A. Purkis, M. D.<br>W. H. Spittel, M. D. |
| Capitol Life Insurance Co. of Colorado, Denver, Colo. | J. M. Foster, M. D. |
| Carolina Life Insurance Co., Columbia, S. C. | C. G. Spivey, M. D. |

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| Central Life Assurance Society, Des Moines, Iowa. | M. I. Olsen, M. D.<br>G. G. Young, M. D. |
| Central Standard Life Ins. Co., Monmouth, Ill. | H. G. Ebersole, M. D. |
| Colonial Life Insurance Co., East Orange, N. J. | L. A. Pyle, M. D. |
| Columbian Mutual Life Ins. Co., Binghamton, N. Y. | R. W. Peterson, M. D. |
| Columbian Mutual Life Ins. Co., Memphis, Tenn. | J. P. Moss, M. D. |
| Columbian National Life Ins. Co., Boston, Mass. | C. H. Kelley, M. D.<br>F. L. Springer, M. D. |
| Columbus Mutual Life Ins. Co., Columbus, Ohio. | F. M. Green, M. D. |
| Commonwealth Life Insurance Co., Louisville, Ky. | A. S. Irving, M. D. |
| Companhia Internacional De Seguros, Rio de Janeiro, Brazil | Luiz Murgel, M. D. |
| Companion Life Ins. Co., New York City | Joseph Altman, M. D. |
| Confederation Life Association, Toronto, Canada. | C. D. Gossage, M. D.<br>G. W. Lougheed, M. D. |
| Connecticut General Life Ins. Co., Hartford, Conn. | N. J. Barker, M. D.<br>L. H. Earle, Jr., M. D.<br>O. G. Goldkamp, M. D.<br>J. D. McGaughey, III, M. D.<br>A. J. Robinson, M. D.<br>K. E. Ward, M. D.<br>A. C. Wilson, M. D. |
| Connecticut Mutual Life Ins. Co., Hartford, Conn. | T. M. Ebers, M. D.<br>H. F. Laramore, M. D.<br>R. E. Nicholson, M. D.<br>D. S. Pepper, M. D.<br>H. B. Rollins, M. D. |

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| Constitution Life Company of America, Los Angeles, Calif. | W. E. Branch, M. D. |
| Continental Amer. Life Ins. Co., Wilmington, Del. | W. M. Genthner, M. D. |
| Continental Assurance Co., Chicago, Ill. | H. W. Dingman, M. D.<br>C. A. Gianasi, M. D.<br>C. J. M. Grisdale, M. D.<br>C. L. Reeder, M. D. |
| Continental Life Insurance Co., Toronto, Canada. | S. J. N. Magwood, M. D. |
| Country Life Insurance Co., Chicago, Ill. | J. E. Boland, M. D. |
| Crown Life Insurance Co., Toronto, Canada. | H. D. Delamere, M. D.<br>F. D. Truax, M. D. |
| Dominion Life Assurance Co., Waterloo, Canada | A. J. McGanity, M. D.<br>J. W. Merritt, M. D. |
| Eastern Life Insurance Co., New York City | Isaac Sossnitz, M. D. |
| Empire Life and Accident Insurance Co., Indianapolis, Ind. | J. M. Leffel, M. D. |
| Empire Life Insurance Co., Kingston, Canada | J. S. Delahaye, M. D. |
| Empire State Mutual Life Insurance Co., Jamestown, N. Y. | C. L. Wilson, M. D. |
| Equitable Life Assurance Society, New York City | R. B. Cleveland, M. D.<br>George Goodkin, M. D.<br>R. S. Graham, M. D.<br>R. S. Gubner, M. D.<br>N. C. Kiefer, M. D.<br>W. C. Lamb, M. D.<br>W. J. McNamara, M. D.<br>Morton Magiday, M. D.<br>W. M. Reynolds, M. D.<br>J. A. Rossa, M. D.<br>W. A. Smith, M. D.<br>H. E. Ungerleider, M. D. |

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| Equitable Life Insurance Co., Washington, D. C. | F. M. McChesney, M. D. |
| Equitable Life Ins. Co. of Canada, Waterloo, Canada | P. G. Schwager, M. D. |
| Equitable Life Insurance Co. of Iowa, Des Moines, Iowa. | W. O. Purdy, M. D.<br>R. R. Simmons, M. D. |
| Excelsior Life Insurance Co., Toronto, Canada. | M. H. Henderson, M. D.<br>B. W. Vale, M. D. |
| Family Fund Life Insurance Company, Atlanta, Ga. | Richard King, M. D. |
| Farm Bureau Life Ins. Co., Columbus, Ohio. | D. E. Yochem, M. D. |
| Farmers & Bankers Life Insurance Co., Wichita, Kan. | C. D. McKeown, M. D. |
| Federal Life and Casualty Company, Battle Creek, Mich. | A. A. Humphrey, M. D. |
| Fidelity Life Assurance Co., Regina, Canada | F. D. Munroe, M. D. |
| Fidelity Mutual Life Ins. Co., Philadelphia, Pa. | J. T. Sheridan, M. D.<br>L. S. Ylvisaker, M. D. |
| Fidelity Union Life Insurance Co., Dallas, Tex. | J. T. Downs, Jr., M. D. |
| First Pyramid Life Insurance Co., Little Rock, Ark. | J. H. Sanderlin, M. D. |
| Franklin Life Ins. Co., Springfield, Ill. | W. A. Henry, M. D.<br>W. F. H. O'Neill, M. D. |
| General American Life Ins. Co., St. Louis, Mo. | J. H. Ready, M. D. |
| Great American Reserve Insurance Co., Dallas, Tex. | G. K. Wallace, M. D. |

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| Great National Life Insurance Co., Dallas, Tex. | P. M. Rattan, M. D. |
| Great Southern Life Insurance Co., Houston, Tex. | F. R. Black, M. D. |
| Great-West Life Assur. Co., Winnipeg, Canada. | A. B. Houston, M. D.<br>F. A. L. Mathewson, M. D.<br>F. H. Smith, M. D. |
| Guarantee Mutual Life Insurance Co., Omaha, Neb. | J. P. Donelan, M. D. |
| Guaranty Income Life Insurance Co., Baton Rouge, La. | H. G. Riche, M. D. |
| Guardian Life Insurance Co. of America, New York City | M. B. Bender, M. D.<br>Phillips Lambkin, M. D.<br>D. C. Roberts, M. D. |
| Gulf Life Insurance Co., Jacksonville, Fla. | J. A. Wilhelm, M. D. |
| Hawaiian Life Insurance Co., Ltd., Honolulu, T. H. | C. E. Fronk, M. D. |
| Home Beneficial Life Insurance Company, Inc., Richmond, Va. | H. M. Goodman, M. D. |
| Home Friendly Insurance Co., Baltimore, Md. | M. Theodore Boss, M. D. |
| Home Life Insurance Co., New York City | J. H. Humphries, M. D.<br>V. L. Karren, M. D.<br>R. J. Oehrig, M. D. |
| Home Life Ins. Co. of America, Philadelphia, Pa. | H. W. Goos, M. D. |
| Home State Life Insurance Co., Oklahoma City, Okla. | W. W. Rucks, M. D. |
| Imperial Life Assurance Co., Toronto, Canada. | J. C. Emmett, M. D.<br>D. L. Selby, M. D. |

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| Independent Order of Foresters, Toronto, Canada | N. S. Clark, M. D. |
| Indianapolis Life Ins. Co., Indianapolis, Ind. | R. M. Nay, M. D. |
| Industrial Life Insurance Co., Quebec, Canada | Maurice Turcotte, M. D. |
| Interstate Life and Accident Co., Chattanooga, Tenn. | J. W. Johnson, Jr., M. D. |
| Jefferson National Life Insurance Co., Indianapolis, Ind. | D. J. Wolfram, M. D. |
| Jefferson Standard Life Ins. Co., Greensboro, N. C. | V. W. Gunter, M. D.<br>H. F. Starr, M. D. |
| John Hancock Mutual Life Ins. Co., Boston, Mass. | R. L. Candage, M. D.<br>B. L. Huntington, M. D.<br>F. J. Kefferstan, II, M. D.<br>J. McC. Peck, M. D.<br>J. L. Tansey, M. D.<br>F. A. Warner, M. D. |
| Kansas City Life Ins. Co., Kansas City, Mo. | G. P. Barnett, M. D.<br>J. E. Bee, M. D. |
| Kentucky Home Mutual Life Insurance Co., Louisville, Ky. | F. M. Stites, M. D. |
| Knights of Columbus, New Haven, Conn. | G. J. Lunz, M. D. |
| "La Latino-Americana", Mexico, D. F. | Ignacio Mesa, M. D. |
| La Nacional, Compania de Seguros Sobre la Vida, S. A., Mexico, D. F. | Aniceto Del Rio, M. D. |
| Liberty Life Insurance Co., Greenville, S. C. | W. S. Fewell, M. D. |

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| Liberty National Life Ins. Co., Birmingham, Ala. | J. A. Livingston, M. D.<br>R. C. Secor, M. D. |
| Life & Casualty Ins. Co. of Tennessee, Nashville, Tenn. | C. T. Kirchmaier, M. D. |
| Life Insurance Co. of Georgia, Atlanta, Ga. | O. E. Hanes, M. D. |
| Life Insurance Co. of Virginia, Richmond, Va. | G. M. Harwood, M. D.<br>H. M. McCue, Jr., M. D.<br>E. S. Williams, M. D. |
| Lincoln Liberty Life Ins. Co., Lincoln, Neb. | G. H. Walker, M. D. |
| Lincoln National Life Ins. Co., Fort Wayne, Ind. | H. A. Cochran, Jr., M. D.<br>I. K. Gardner, M. D.<br>G. M. Graham, M. D.<br>J. L. Humphreys, M. D.<br>W. H. Scoins, M. D. |
| London Life Insurance Co., London, Canada. | J. T. Bowman, M. D.<br>G. R. Collyer, M. D.<br>A. S. Graham, M. D.<br>J. S. Winder, M. D. |
| Loyal Protective Life Insurance Co., Boston, Mass. | H. W. Hudson, M. D. |
| Lutheran Brotherhood, Minneapolis, Minn. | H. J. Brekke, M. D. |
| Maccabees (The), Detroit, Mich. | H. R. John, M. D. |
| Manhattan Life Insurance Co., New York City | L. G. LaPointe, M. D. |
| Manufacturers Life Ins. Co., Toronto, Canada. | D. J. Breithaupt, M. D.<br>T. C. Dunlop, M. D.<br>H. M. Gray, M. D.<br>R. C. Montgomery, M. D. |
| Maritime Life Insurance Co., Halifax, Canada | G. H. Murphy, M. D. |

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| Massachusetts Mutual Life Insurance Co., Springfield, Mass. | H. B. Brown, M. D.<br>J. R. E. Morden, M. D.<br>Gordon Ross, M. D.<br>T. S. Sexton, M. D.<br>B. L. Wales, Jr., M. D. |
| Metropolitan Life Insurance Co., New York City | Henry Almond, M. D.<br>E. F. Beach, Ph. D.<br>D. M. Benford, M. D.<br>R. A. Benson, M. D.<br>C. C. Berwick, M. D.<br>E. C. Bonnett, M. D.<br>A. W. Bromer, M. D.<br>E. T. Dewey, M. D.<br>R. K. Farnham, M. D.<br>H. H. Fellows, M. D.<br>R. W. Finegan, M. D.<br>J. G. Forgerson, M. D.<br>J. T. Geiger, M. D.<br>J. C. Horan, M. D.<br>A. O. Jimenis, M. D.<br>H. B. Kidd, M. D.<br>W. J. McConnell, M. D.<br>G. S. Pesquera, M. D.<br>G. P. Robb, M. D.<br>K. J. Thomson, M. D.<br>Wallace Troup, M. D. |
| Michigan Life Insurance Co., Detroit, Mich. | **R. J. Scott, M. D.** |
| Midland Mutual Life Insurance Co., Columbus, Ohio | **P. H. Charlton, M. D.** |
| Midland National Life Insurance Co., Watertown, S. D. | O. S. Randall, M. D. |
| Midwest Life Insurance Co., Lincoln, Neb. | E. W. Rowe, M. D. |
| Minnesota Mutual Life Insurance Co., St. Paul, Minn. | W. F. Larrabee, Jr., M. D.<br>A. E. Venables, M. D. |

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| Missouri Insurance Co., St. Louis, Mo. | C. D. Magee, M. D. |
| Modern Woodmen of America, Rock Island, Ill. | E. A. Anderson, M. D. |
| Monarch Life Assur. Co., Winnipeg, Canada | J. P. Gemmell, M. D. |
| Monarch Life Insurance Co., Springfield, Mass. | L. E. Hathaway, Jr., M. D.<br>H. N. Simpson, M. D. |
| Montreal Life Insurance Co., Montreal, Canada | R. V. Ward, M. D. |
| Monumental Life Insurance Co., Baltimore, Md. | F. H. Vinup, M. D. |
| Mutual Benefit Life Insurance Co., Newark, N. J. | J. R. Beard, M. D.<br>E. C. Hillman, Jr., M. D.<br>M. T. Ryman, M. D.<br>D. F. Steuart, M. D.<br>Jefferson Weed, M. D. |
| Mutual Life Assur. Co. of Canada, Waterloo, Canada | R. H. Craig, M. D.<br>J. G. Ross, M. D.<br>R. W. Zinkann, M. D. |
| Mutual Life Ins. Co. of New York, New York City | J. R. Gudger, M. D.<br>T. J. McGurl, Jr., M. D.<br>J. F. Moore, Jr., M. D.<br>S. A. Narins, M. D.<br>T. E. Plucinski, M. D.<br>A. A. Pollack, M. D.<br>R. L. Willis, M. D. |
| Mutual Trust Life Insurance Co., Chicago, Ill. | R. B. Schlesinger, M. D.<br>A. A. Willander, M. D. |
| National Equity Life Insurance Co., Little Rock, Ark. | Alfred Kahn, Jr., M. D. |
| National Guardian Life Insurance Co., Madison, Wis. | A. R. Tormey, M. D. |

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| National Life & Accident Ins. Co., Nashville, Tenn. | B. F. Byrd, M. D.<br>G. E. Fort, M. D.<br>L. C. Miller, M. D. |
| National Life Assurance Co. of Canada, Toronto, Canada | D. B. Campbell, M. D. |
| National Life Co., Des Moines, Iowa | L. K. Meredith, M. D. |
| National Life Insurance Co., Montpelier, Vt. | H. L. Colombo, M. D.<br>M. G. MacDonald, M. D.<br>J. L. Saia, M. D. |
| National Old Line Insurance Co., Little Rock, Ark. | R. E. McLochlin, M. D. |
| National Reserve Life Insurance Co., Sioux Falls, S. D. | Rezin Reagan, M. D |
| New England Mutual Life Ins. Co., Boston, Mass. | F. R. Brown, M. D.<br>M. H. Clifford, M. D.<br>O. C. Hendrix, M. D.<br>W. F. Ketchum, M. D.<br>R. B. Singer, M. D. |
| New York Life Insurance Co., New York City | D. R. Auten, M. D.<br>M. F. Bell, M. D.<br>William Bolt, M. D.<br>E. J. Campbell, M. D.<br>G. D. Dorman, M. D.<br>A. H. Faber, M. D.<br>E. M. Freeland, M. D.<br>E. E. Getman, M. D.<br>H. L. Hauge, M. D.<br>T. B. Hoxie, M. D.<br>J. J. Hutchinson, M. D.<br>I. C. Lawler, M. D.<br>John Malgieri, M. D.<br>D. J. O'Leary, M. D.<br>R. W. Pratt, M. D.<br>L. J. Tedesco, M. D. |
| North American Life Assur. Co., Toronto, Canada | J. G. Falconer, M. D.<br>Eugene Montgomery, M. D. |

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| North American Reassurance Co., New York City | E. V. Higgins, M. D. |
| Northern Life Assurance Co. of Canada, London, Canada | J. H. Geddes, M. D. |
| Northwestern Mutual Life Ins. Co., Milwaukee, Wis. | R. W. Benton, M. D.<br>J. M. Bond, M. D.<br>J. A. End, M. D.<br>D. F. Rikkers, M. D.<br>J. R. Slamer, M. D.<br>G. F. Tegtmeyer, M. D.<br>A. R. Zintek, M. D. |
| Northwestern National Life Ins. Co., Minneapolis, Minn. | K. W. Anderson, M. D. |
| Norwich Union Life Insurance Society, Toronto, Canada | W. B. Thornton, M. D. |
| Occidental Life Ins. Co. of California, Los Angeles, Calif. | E. F. Sheldon, M. D.<br>Joseph Travenick, Jr., M. D. |
| Ohio National Life Ins. Co., Cincinnati, Ohio | H. H. Shook, M. D.<br>B. W. Sitterson, M. D. |
| Ohio State Life Insurance Co., Columbus, Ohio | T. F. Ross, M. D. |
| Old Line Life Insurance Co. of America, Milwaukee, Wis. | H. M. Hawkins, M. D.<br>R. D. O'Connor, M. D. |
| Oriental Government Security Life Assurance Co., Ltd., Bombay, India. | K. J. J. Cursetji, M. D. |
| Pacific Mutual Life Ins. Co., Los Angeles, Calif. | F. R. Anderson, M. D.<br>L. H. Lee, M. D.<br>J. C. Talbot, M. D. |
| Pan-American Life Ins. Co., New Orleans, La. | R. C. Voss, M. D. |

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| Paul Revere Life Ins. Co., Worcester, Mass. | E. R. Lamb, M. D.<br>H. R. Leffingwell, M. D.<br>J. K. Ruggles, Jr., M. D. |
| Penn Mutual Life Ins. Co., Philadelphia, Pa. | J. R. Bowen, M. D.<br>B. A. Dawber, M. D.<br>E. S. Dillon, M. D.<br>D. W. Hoare, M. D.<br>W. R. Leute, Jr., M. D.<br>R. L. Weaver, M. D. |
| Peoples Life Insurance Co., Frankfort, Ind. | C. A. Burroughs, M. D. |
| Peoples Life Insurance Co., Washington, D. C. | M. A. Puzak, M. D. |
| Philadelphia Life Ins. Co., Philadelphia, Pa. | T. M. Armstrong, M. D. |
| Phoenix Mutual Life Ins. Co., Hartford, Conn. | W. R. Bradley, M. D.<br>H. B. Campbell, M. D.<br>R. A. Goodell, M. D.<br>Llewellyn Hall, M. D.<br>N. R. Kelley, M. D. |
| Pilot Life Insurance Co., Greensboro, N. C. | J. L. Cook, M. D. |
| Pioneer Mutual Life Insurance Co., Fargo, N. D. | F. O. Gronvold, M. D. |
| Postal Life Insurance Co., New York City | L. B. Dunn, M. D. |
| Preferred Life Assurance Society, Montgomery, Ala. | B. C. Bird, M. D. |
| Protected Home Circle, Sharon, Pa. | W. G. McLaughry, M. D. |
| Protective Life Insurance Co., Birmingham, Ala. | E. G. Givhan, Jr., M. D. |
| Provident Life and Accident Ins. Co., Chattanooga, Tenn. | W. R. Bishop, M. D. |

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| Provident Mutual Life Ins. Co., Philadelphia, Pa. | E. J. Brogan, M. D.<br>P. H. Langner, Jr., M. D.<br>L. L. McLellan, M. D.<br>S. R. Moore, M. D. |
| Prudential Assur. Co., Ltd., Montreal, Canada | E. S. Mills, M. D.<br>C. A. Peters, M. D. |
| Prudential Insurance Co. of America, Newark, N. J. | S. F. Bassett, M. D.<br>R. F. Buchan, M. D.<br>E. G. Dewis, M. D.<br>A. H. Domm, M. D.<br>V. J. Donnelly, M. D.<br>R. L. Dross, M. D.<br>J. C. Fitzpatrick, M. D.<br>R. E. Funke, M. D.<br>F. I. Ganot, M. D.<br>A. E. Gras, M. D.<br>W. C. Hausheer, M. D.<br>E. G. Howe, M. D.<br>E. A. Keenleyside, M. D.<br>C. E. Kiessling, M. D.<br>H. B. Kirkland, M. D.<br>N. L. Knott, M. D.<br>J. C. Lindner, M. D.<br>F. J. McGurl, M. D.<br>P. V. Martin, M. D.<br>R. A. Nelson, M. D.<br>A. J. Oberlander, M. D.<br>W. C. Page, M. D.<br>P. V. Reinartz, M. D.<br>R. C. Roadhouse, M. D.<br>R. S. Schaaf, M. D.<br>K. F. Schaefer, M. D. |
| Puritan Life Insurance Co., Providence, R. I. | E. D. Chesebro, M. D. |
| Republic National Life Ins. Co., Dallas, Tex. | J. E. Hunsinger, M. D.<br>D. G. Kilgore, M. D. |
| Reserve Life Insurance Co., Dallas, Tex. | D. W. Carter, Jr., M. D. |
| Rockford Life Insurance Co., Rockford, Ill. | P. A. Anderson, M. D. |

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| **Royal Insurance Co., Ltd., Montreal, Canada** | G. W. Halpenny, M. D. |
| **Security Benefit Life Ins. Co., Topeka, Kan.** | F. R. Stearns, M. D. |
| Security Life and Accident Co., Denver, Colo. | D. S. Baughman, M. D.<br>R. C. Scannell, M. D. |
| Security Life & Trust Co., Winston-Salem, N. C. | S. W. Hurdle, M. D. |
| **Security Mutual Life Ins. Co., Binghamton, N. Y.** | W. B. Aten, M. D.<br>V. G. Hammond, M. D. |
| **Shenandoah Life Insurance Co., Inc., Roanoke, Va.** | D. S. Garner, M. D. |
| Southern Life Insurance Co. of Georgia, Atlanta, Ga. | D. Y. Sage, M. D. |
| Southland Life Insurance Co., Dallas, Tex. | Hall Shannon, M. D. |
| **Southwestern Life Ins. Co., Dallas, Tex.** | C. F. Brown, M. D.<br>C. E. Cook, M. D. |
| Sovereign Life Assurance Co., Winnipeg, Canada | C. P. Neilson, M. D. |
| **Standard Insurance Company, Portland, Ore.** | E. L. Boylen, M. D. |
| Standard Life Association, Lawrence, Kan. | G. D. Townshend, M. D. |
| **Standard Life Assur. Co., Montreal, Canada** | W. W. Eakin, M. D. |
| State Farm Life Insurance Co., Bloomington, Ill. | J. T. France, M. D.<br>E. M. Stevenson, M. D. |
| **State Mutual Life Assur. Co., Worcester, Mass.** | F. P. Bicknell, M. D. |
| State Reserve Life Insurance Co., Fort Worth, Tex. | Samuel Jagoda, M. D. |

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| Sun Life Assurance Company of Canada, Montreal, Canada | J. K. Gordon, M. D.<br>D. H. Woodhouse, M. D.<br>A. W. Young, M. D. |
| Sun Life Insurance Co. of America, Baltimore, Md. | George McLean, M. D. |
| Sunset Life Insurance Co. of America, Olympia, Wash. | J. E. Toothaker, M. D. |
| Teachers Insurance & Annuity Association, New York City | William MacDonald, M. D. |
| T. Eaton Life Assurance Co., Toronto, Canada | C. V. Mulligan, M. D. |
| Texas Life Insurance Co., Waco, Tex. | I. E. Colgin, M. D. |
| Texas Prudential Insurance Co., Galveston, Tex. | E. R. Thompson, M. D. |
| Toronto Mutual Life Ins. Co., Toronto, Canada | J. A. A. Harcourt, M. D. |
| Travelers Insurance Company, Hartford, Conn. | R. M. Filson, M. D.<br>A. L. Larson, M. D.<br>C. B. LeRoyer, Jr., M. D.<br>J. C. Robinson, M. D.<br>A. F. Seibert, M. D.<br>V. H. Young, M. D. |
| Union Central Life Insurance Co., Cincinnati, Ohio | W. D. Hickerson, M. D.<br>Edward Kuck, M. D.<br>Louis Schwab, M. D. |
| Union Labor Life Insurance Co., New York City | W. L. O'Connell, M. D. |
| Union Life Insurance Co., Little Rock, Ark. | J. H. Hayes, M. D. |
| Union Mutual Life Insurance Co., Portland, Me. | H. E. Christensen, M. D. |

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| United Benefit Life Insurance Co., Omaha, Neb. | N. L. Criss, M. D. |
| United Fidelity Life Insurance Co., Dallas, Tex. | H. K. Crutcher, M. D. |
| United Life and Accident Ins. Co., Concord, N. H. | P. M. L. Forsberg, M. D. |
| United Life Insurance Co., Jacksonville, Fla. | J. F. Lovejoy, M. D. |
| United States Life Ins. Co., New York City | C. M. Bonzey, Jr., M. D. |
| Victory Life Insurance Co., Topeka, Kan. | M. B. Miller, M. D. |
| Volunteer State Life Ins. Co., Chattanooga, Tenn. | F. F. Harris, M. D. |
| Washington National Insurance Company, Evanston, Ill. | P. C. Waldo, M. D. |
| West Coast Life Ins. Co., San Francisco, Calif. | I. C. Heron, M. D. |
| Western Life Assurance Company, Hamilton, Canada | G. E. Greenway, M. D. |
| Western Life Insurance Company, Helena, Mont. | T. L. Hawkins, M. D.<br>E. H. Lindstrom, M. D. |
| Western and Southern Life Ins. Co., Cincinnati, Ohio | C. M. Barrett, M. D.<br>M. W. Gwinner, M. D.<br>F. A. Snyder, M. D. |
| Western States Life Insurance Company, Fargo, N. D. | T. H. Lewis, M. D. |
| Wisconsin Life Insurance Company, Madison, Wis. | G. G. Stebbins, M. D. |

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| Wisconsin National Life Insurance Company, Oshkosh, Wis. | E. B. Williams, M. D. |
| Woodmen of the World Life Insurance Society, Omaha, Neb. | H. B. Kennedy, M. D. |
| Workmen's Benefit Fund, Brooklyn, N. Y. | Abraham Block, M. D. |

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